MHIF FEATURED STUDY:

Myocardial perfusion and contraction assessed by cardiac MRI in acute and recovery takotsubo syndrome

OPEN AND ENROLLING* / EPIC message: *Research MHIF Patient Referral

CONDITION:
Takotsubo syndrome (TS)

PI: Retu Saxena, MD
Co-I: Scott Sharkey, MD

RESEARCH CONTACTS:
Steph Ebnet
stephanie.ebnet@allina.com | 320-291-8950
Sarah Schwager
sarah.schwager@allina.com | 319-350-9643

SPONSOR:
MHIF IIR

DESCRIPTION: This study will use the new respiratory motion-corrected automated in-line perfusion mapping stress CMR protocol to quantify regional myocardial blood flow (MBF) and myocardial perfusion reserve (MPR) in TS patients resulting in a "myocardial perfusion map" which can be correlated with a "myocardial contraction map."

CRITERIA LIST/ QUALIFICATIONS:

Inclusion:

- Admitted with acute TS without significant coronary artery obstruction as defined on invasive coronary angiogram or CT coronary angiogram
- Typical apical or mid-ventricular ballooning pattern based on initial echocardiogram or left ventriculogram
- Age > 18 years

Exclusion:

- Significant acute or chronic renal disease (dialysis or estimated glomerular filtration rate <30 ml/min/m2)
- Contraindication to adenosine or gadolinium
- Decompensated acute heart failure (need for mechanical ventilation, vasopressor treatment of hypotension, mechanical circulatory support)
- Pregnancy or lactation
- Atrial fibrillation or sustained ventricular tachycardia/ventricular fibrillation
- Asthma requiring hospitalization or oxygen dependent COPD
- Bradycardia or advanced heart block unless pacemaker present

HOPE DISCOVERED HERE™

Minneapolis Heart Institute Foundation®
Creating a world without heart and vascular disease

Adult Presentation of Congenital Heart Disease

Christina Thaler, MD PhD

HOPE DISCOVERED HERE

Minneapolis Heart Institute Foundation

1

- No conflicts of interest

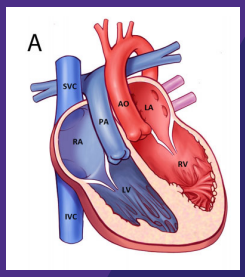
HOPE DISCOVERED HERE

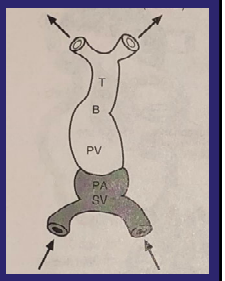
Minneapolis Heart Institute Foundation

2

Definition of Adult Congenital Heart Disease

- Structural heart disease present prior to birth
- Attributed to abnormal fetal development
- Does NOT include heritable diseases
  - Marfan Syndrome
  - Hypertrophic Cardiomyopathy
  - Arrhythmogenic Ventricular Dysplasia





Kutty, S., et al. (2018). Contemporary management and outcomes in congenitally corrected transposition of the great arteries. *Heart*, *104*(14), 1148-1155.
Dudek, R. W. (2013). *High-yield embryology*. Lippincott Williams & Wilkins.

3

ACHD Classification

CHD Anatomy

- Simple
- Moderate Complexity
- Great Complexity

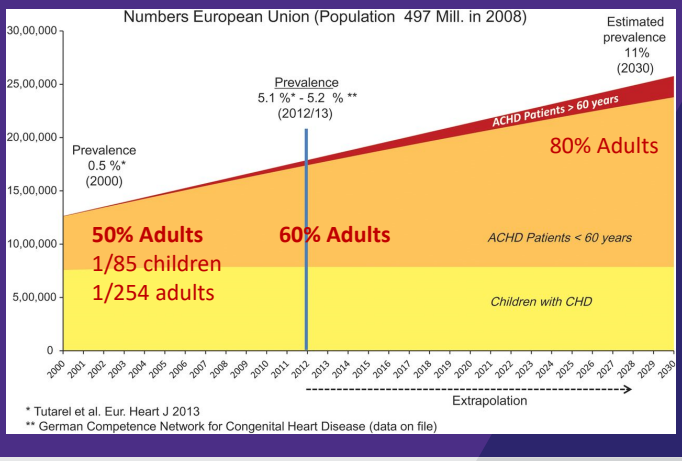
CHD Physiology

- A: No symptoms / physiologic consequence
- B: NYHA Class II symptoms, mild physiological consequences
- C: NYHA Class III symptoms, moderate physiological consequences
- D: NYHA Class IV symptoms: severe / end stage physiological consequences

4

Prevalence of CHD in the European Union

2000:
0.8 - 1.3 million adults
with CHD in the US



Helmut Baumgartner Eur Heart J 2014;35:683-685

5

ACHD Presenting in Adulthood

- 1% of Korean patients at an academic medical center with an elective echocardiogram performed prior to a physical exam

Table 3 Distribution of newly diagnosed congenital heart diseases (CHD, $n = 293$ cases)

	Numbers of CHD (%)	Male/Female (n = cases)
Bicuspid aortic valve	155(52.9%)	106/49
Atrial septal defect	102 (34.8%)	27/75
Ventricular septal defect	14 (4.78%)	9/5
Pulmonary stenosis	12 (4.09%)	5/7
Patent ductus arteriosus	8 (2.73%)	6/2
Coarctation of Aorta	3 (1.02%)	2/1
Partial anomalous of pulmonary venous returns	2 (0.68%)	1/1
Cor triatriatum	7 (2.39%)	3/4
Ebstein's anomaly	5 (1.71%)	1/4
Congenitally corrected transposition of great arteries	2 (0.68%)	0/2

Kwag, E. M., Lee, J. S., & Kim, S. H. (2018). The incidentally diagnosed adult congenital heart disease during routine medical health checkups in 27,897 Koreans at a single center over seven years. *BMC Cardiovascular Disorders*, *18*(1), 223.

6

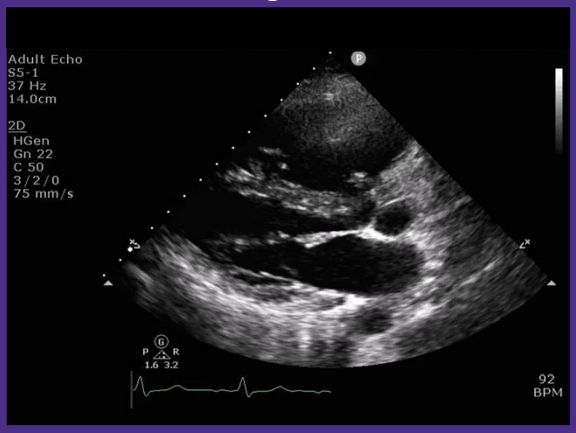
29 year old pregnant woman with tachycardia

- Referred to cardiology during her second semester of pregnancy due to resting tachycardia with HR 110s and dyspnea on exertion
- BP 104/68, HR 106, RR 20 in clinic
- Noted to have a soft murmur at right upper sternal border
- Echocardiogram obtained

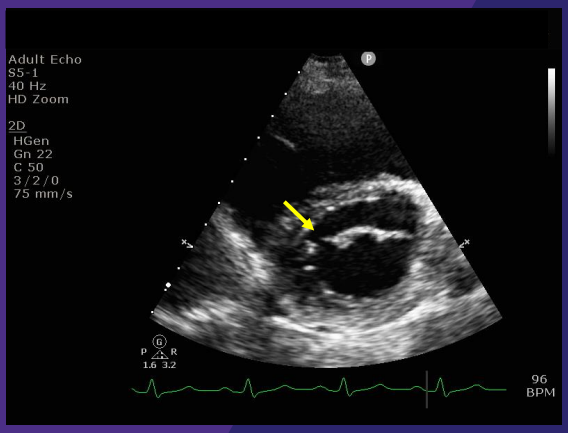
HOPE DISCOVERED HERE | Minneapolis Heart Institute Foundation

7

Enlarged RV



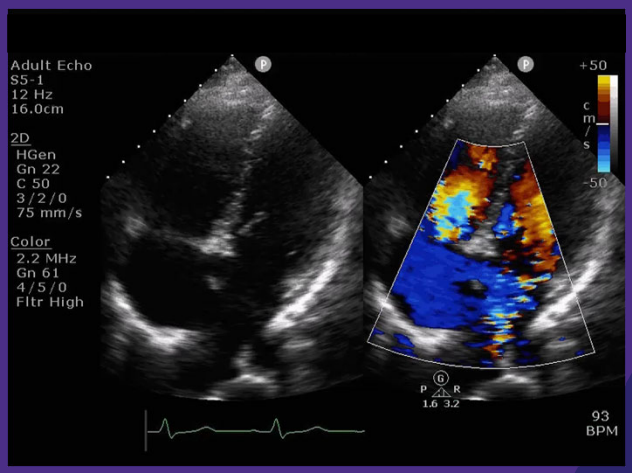
Cleft Mitral Valve



HOPE DISCOVERED HERE | Minneapolis Heart Institute Foundation

8

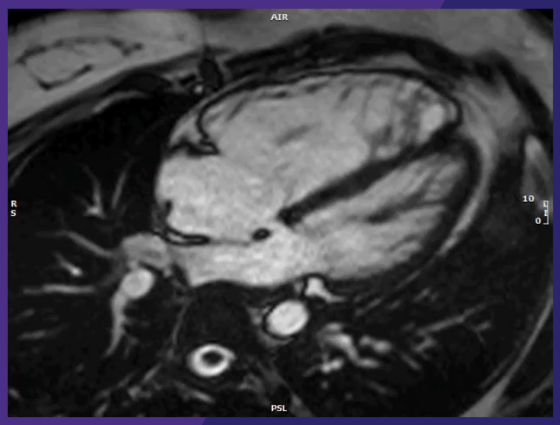
Left to Right Shunting Across an Atrial Septal Defect



9

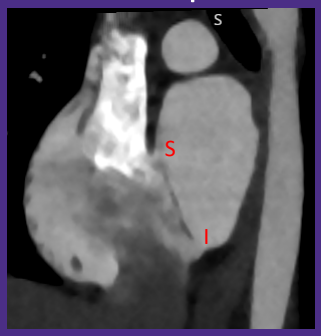
cMRI

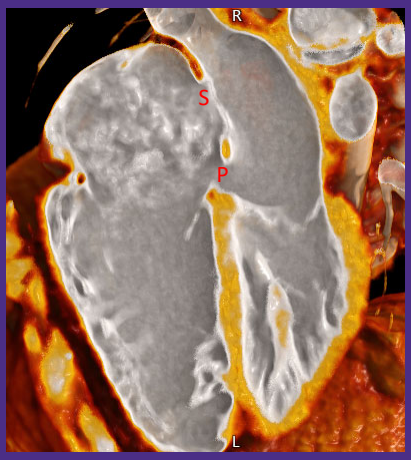
- Qp:Qs Shunt of 2.3:1
- Preserved LV and RV function
- Enlarged RV
  - EDV 117 ml/m2 (normal 61-98 ml/m2)
- Complex ASD Noted

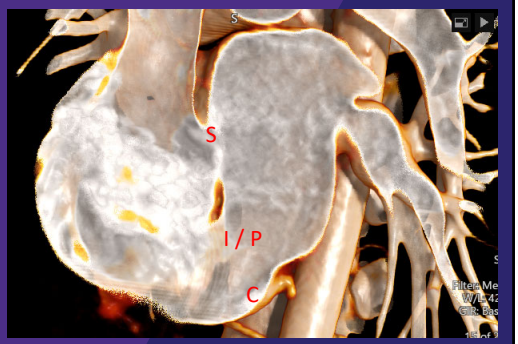


10

Complex Atrial Septal Defect







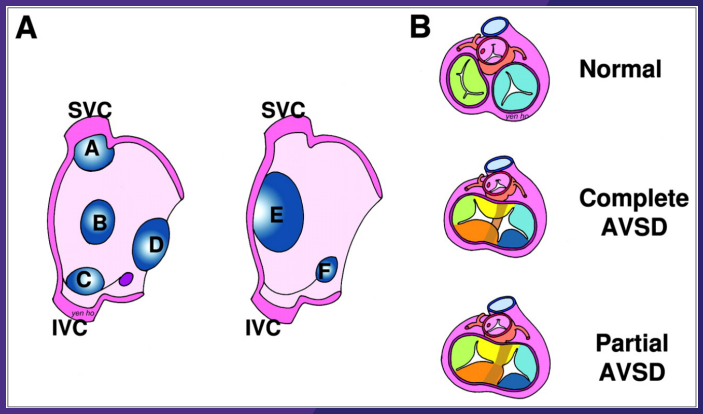
S: Secundum ASD
I: Inferior Sinus Venosus ASD
P: Ostium Primum ASD
C: Coronary Sinus ASD

HOPE DISCOVERED HERE
Minneapolis Heart Institute Foundation

11

Types of ASD

- A: Superior sinus venosus ASD
- B: Secundum ASD
- C: Inferior sinus venosus ASD
- D: Ostium primum ASD
- E: Secundum ASD without posterior septal rim
- F: Coronary sinus ASD



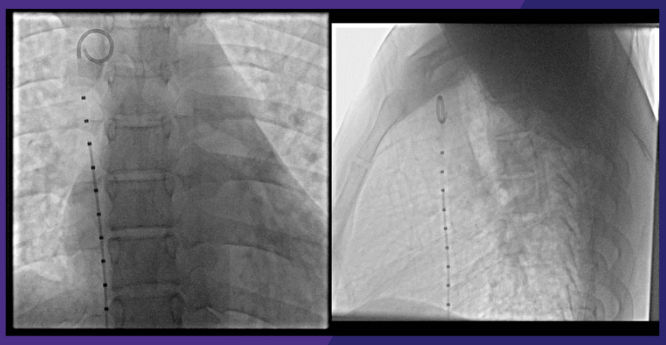
Gary Webb, and Michael A. Gatzoulis Circulation. 2006;114:1645-1653

HOPE DISCOVERED HERE
Minneapolis Heart Institute Foundation

12

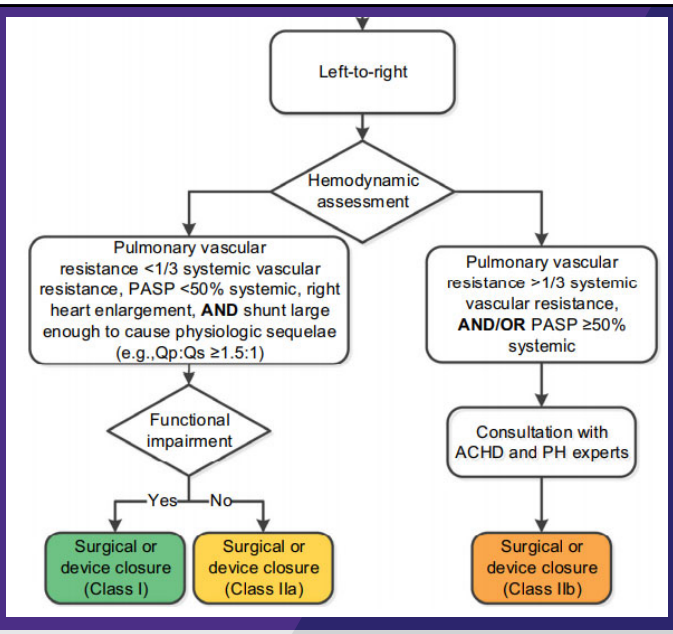
Right Heart Catheterization

- Normal right sided filling pressures
  - RA=6
  - RV=38/9
  - PA=32/11, mean 20
- Normal left sided filling pressures
  - PCWP 8mmHg
- Qp/Qs= 1.8



13

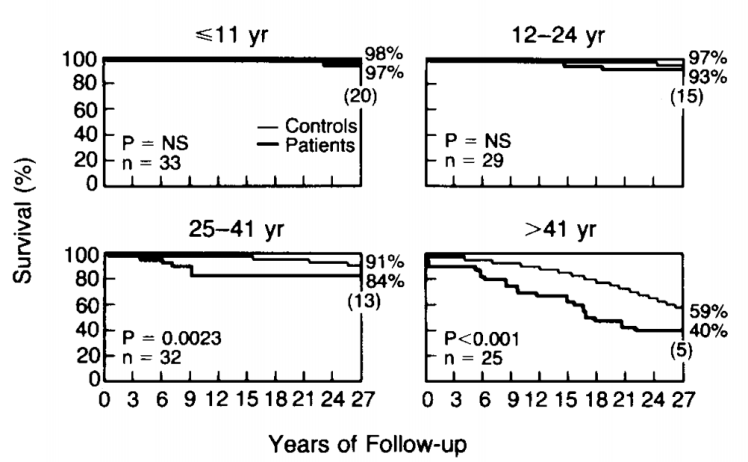
ASD Closure



Stout, K. K., et al. (2019). 2018 AHA/ACC guideline for the management of adults with congenital heart disease: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Journal of the American College of Cardiology*, *73*(12), 1494-1563.

14

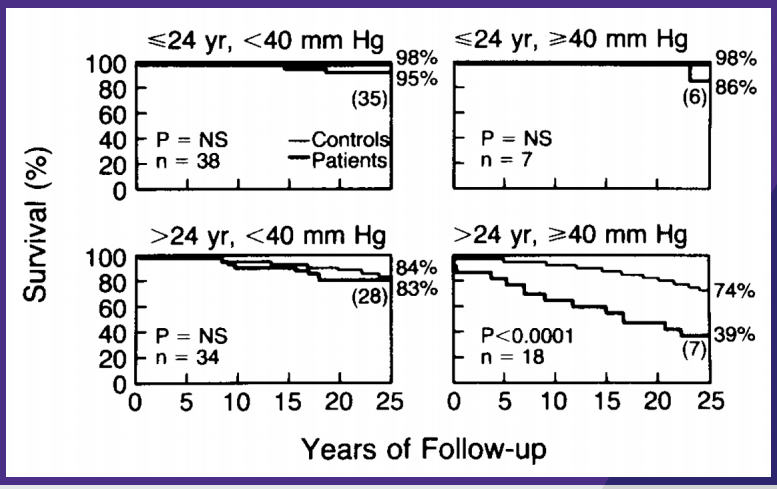
Younger Age of Closure Has Improved Survival



Murphy, J. G. et al. (1990). Long-term outcome after surgical repair of isolated atrial septal defect: follow-up at 27 to 32 years. *New England Journal of Medicine*, *323*(24), 1645-1650.

15

Worse Survival With Elevated Systolic PA Pressures > 40mmHg



Murphy, J. G. et al. (1990). Long-term outcome after surgical repair of isolated atrial septal defect: follow-up at 27 to 32 years. *New England Journal of Medicine*, *323*(24), 1645-1650.

16

Cardiac Complications Following Surgery

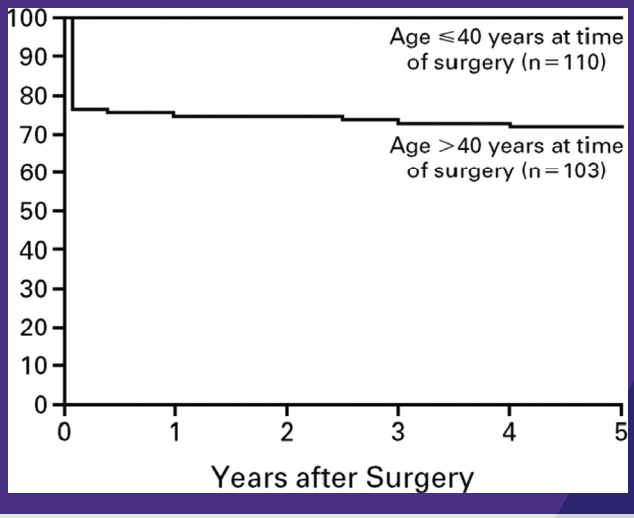
Table 2. Summary of Late Cardiac Events According to Age at Operation.

Event	≤24 Yr (N = 62)	>24 Yr (N = 61)
Stroke	0	8
Transient ischemic attacks	0	2
Heart failure	2	15
Complete heart block	0	2
Implantation of permanent pacemaker	2	3
Valvular heart surgery	1	1
Reoperation for atrial septal defect	1	0
Myocardial infarction	0	4
Infective endocarditis	2	0
Pericarditis	1	0
Total	9 (15%)	35 (57%)

Murphy, J. G. et al. (1990). Long-term outcome after surgical repair of isolated atrial septal defect: follow-up at 27 to 32 years. *New England Journal of Medicine*, *323*(24), 1645-1650.

17

Arrhythmia by age of ASD Closure

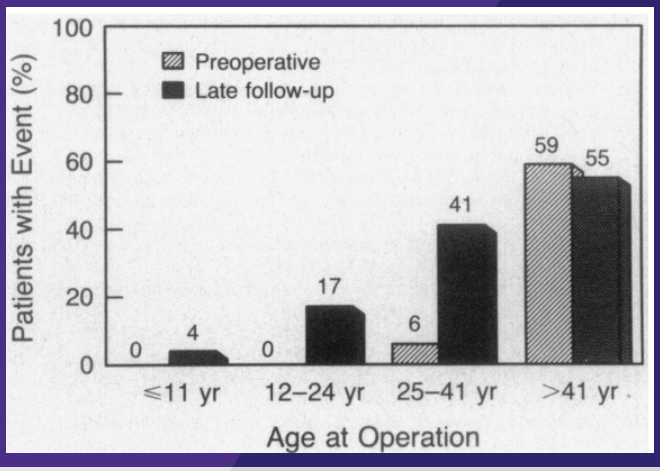


Gatzoulis, M. A., Freeman, M. A., Siu, S. C., Webb, G. D., & Harris, L. (1999). Atrial arrhythmia after surgical closure of atrial septal defects in adults. *New England Journal of Medicine*, *340*(11), 839-846.

18

Atrial Fibrillation / Atrial Flutter

- Mayo cohort study 22% of late deaths were secondary to stroke
  - All patients had Atrial flutter / fibrillation
- Danish Registry Study 22% developed atrial fibrillation with closure < 24 years

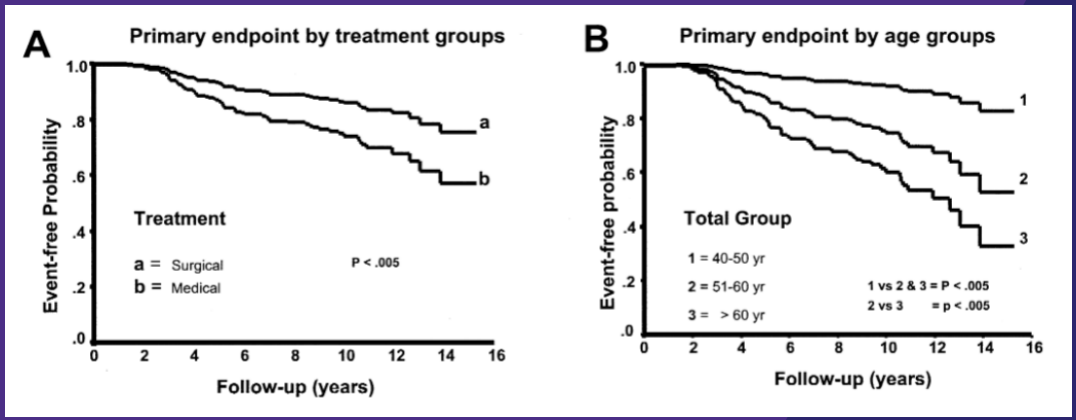


Murphy, J. G. et al. (1990). Long-term outcome after surgical repair of isolated atrial septal defect: follow-up at 27 to 32 years. *New England Journal of Medicine*, *323*(24), 1645-1650.

Nyboe, C., Olsen, M. S., Nielsen-Kudsk, J. E., & Hjortdal, V. E. (2015). Atrial fibrillation and stroke in adult patients with atrial septal defect and the long-term effect of closure. *Heart*, *101*(9), 706-711.

19

Surgical Treatment Superior to Medical In Patients Over 40 years



Primary Endpoint was the first presentation of either: death, pulmonary embolism, major arrhythmic event, embolic cerebrovascular event, recurrent pulmonary infection, functional class deterioration or heart failure

Attie, F., et al. (2001). Surgical treatment for secundum atrial septal defects in patients> 40 years old: a randomized clinical trial. *Journal of the American College of Cardiology*, *38*(7), 2035-2042.

20

Anticoagulation with Atrial Fibrillation and Congenital Heart Disease

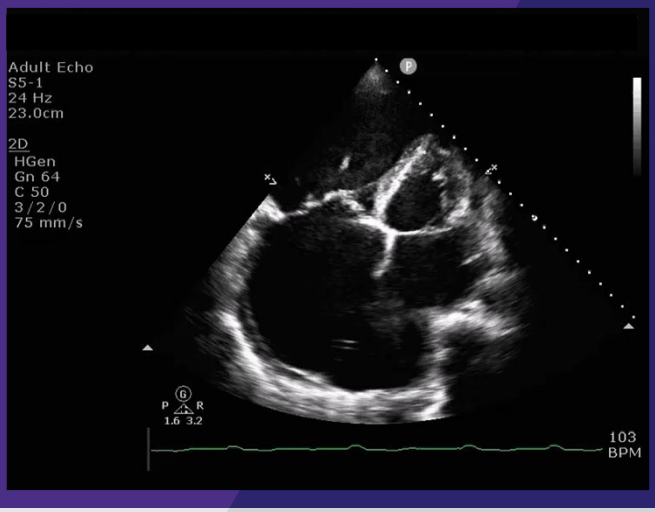
- 2016 and 2020 ESC Guidelines for Anticoagulation
  - Standard atrial fibrillation risk assessment (CHADS2 Vasc Score)
  - Intra-cardiac repair

Hindricks, G. et al. (2020). 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association of Cardio-Thoracic Surgery (EACTS). *European heart journal*. 00: 1-126

21

Eisenmenger Syndrome

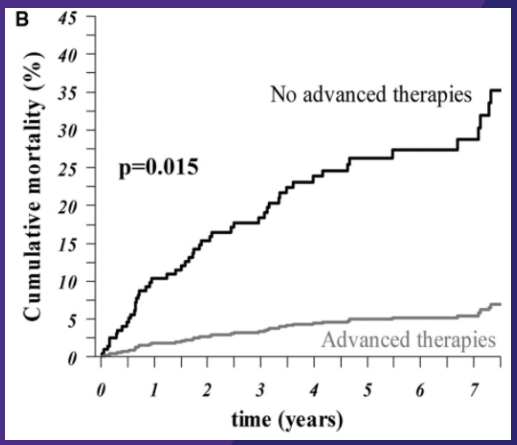
- 54 year old woman with atrial fibrillation and NYHA class III-IV symptoms
- Declined medical treatment other than rate controlling medication and diuretics
- Died 3 years after initial presentation



22

Survival improved with advanced therapies

- Bosentan : class I indication
- PDE-5 inhibitors: Class IIa indication
- Bosentan and PD5-inhibitor: Class IIa recommendation
- Oxygen and anticoagulation can be considered
- ASD closure is contraindicated



Dimopoulos, K. et al. (2009). Improved Survival Amongst Patients With Eisenmenger Syndrome Receiving Advanced Therapy for Pulmonary Arterial Hypertension.

23

All Patients with ASD Should Have Life Long Cardiology Follow-up

- Atrial arrhythmias
  - Anticoagulation for atrial fibrillation / flutter if has had prior ASD closure
- Change in shunt size
- Pulmonary hypertension
- Heart Failure

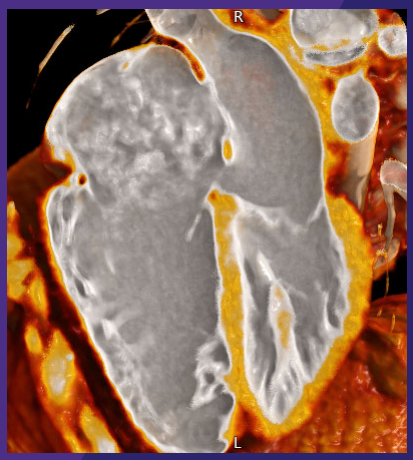
Frequency of Routine Follow-Up and Testing	Physiological Stage A* (mo)	Physiological Stage B* (mo)	Physiological Stage C* (mo)	Physiological Stage D* (mo)
Outpatient ACHD cardiologist	36-60	24	6-12	3-6
ECG	36-60	24	12	12
TTE	36-60	24	12	12
Pulse oximetry	As needed	As needed	Each visit	Each visit
Exercise test†	As needed	As needed	12-24	6-12

Stout, K. K., et al. (2019). 2018 AHA/ACC guideline for the management of adults with congenital heart disease: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Journal of the American College of Cardiology*, *73*(12), 1494-1563.

24

Atrial Septal Defect Summary

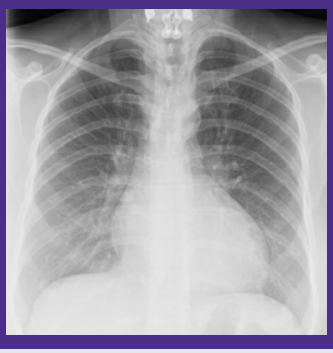
- One of the more common ACHD conditions to present in adulthood
- Survival is reduced with late closure
- Percutaneous closure is only for secundum ASDs
- Atrial fibrillation, heart failure and stroke are the most common complications following closure

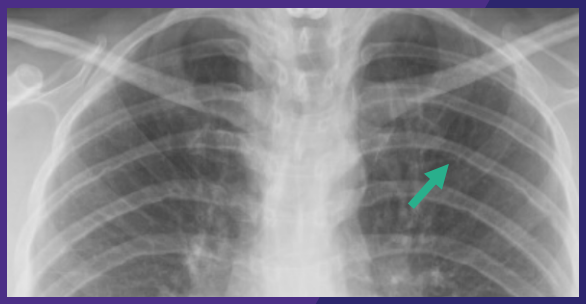


25

45 year old woman with longstanding hypertension diagnosed during pregnancy

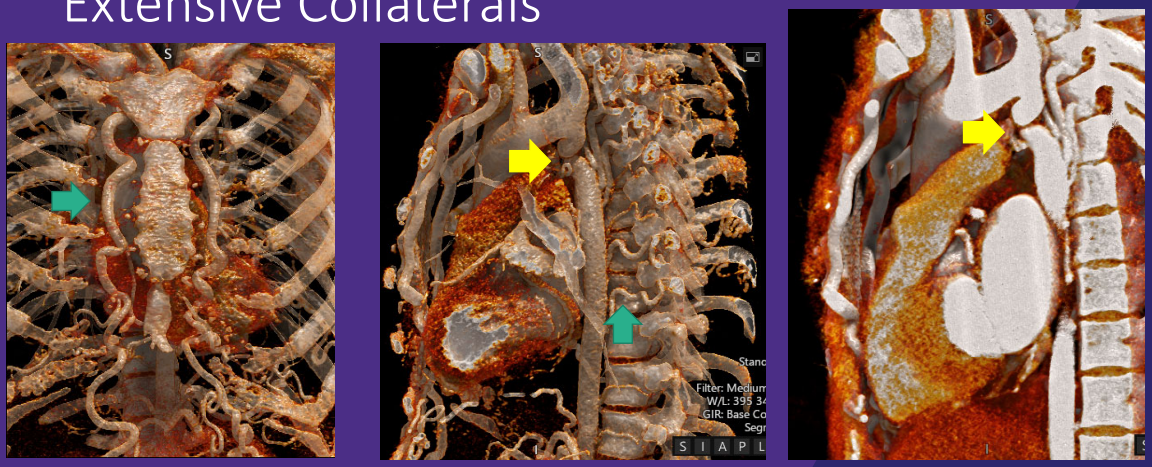
- Presented to primary care with new onset of dyspnea on exertion and atypical chest pain





26

Severe Coarctation of The Aorta With Extensive Collaterals

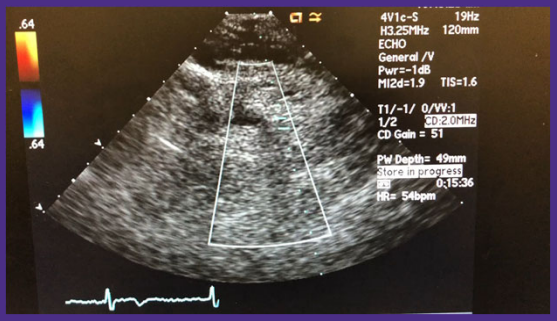


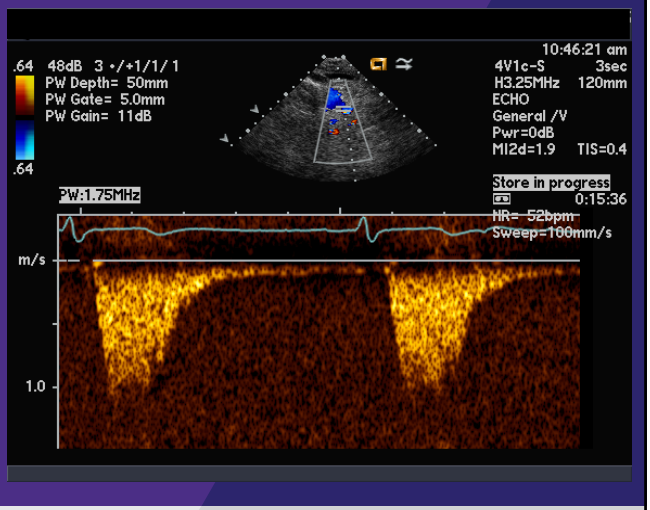
HOPE DISCOVERED HERE

Minneapolis Heart Institute Foundation

27

Coarctation of the Aorta on Echocardiogram





HOPE DISCOVERED HERE

Minneapolis Heart Institute Foundation

28

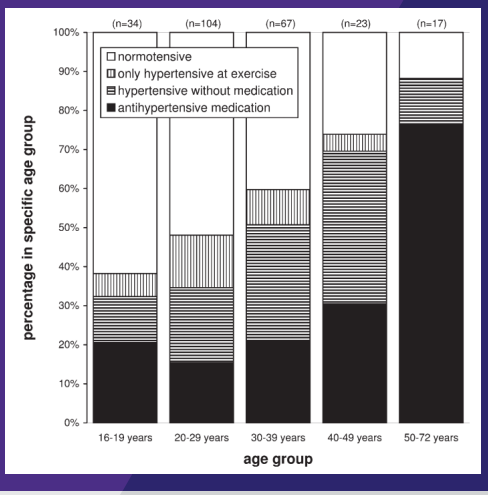
Further History

- Symptomatic claudication during walking
- BP 142/71 upper extremity, systolic 98 in lower extremity bilaterally
- Underwent surgical repair with an 18mm interposition graft in the proximal descending aorta
- Subsequently lost to cardiology follow-up

29

Hypertension in Common And Increases With Age

- Monitoring
  - Resting blood pressure in upper and lower extremities (Class I recommendation)
  - Ambulatory monitoring (Class IIa recommendation)
  - Exercise blood pressure assessment (Class IIb recommendation)
- Often Undertreated
  - UK Cohort Study only 18% appropriately treated

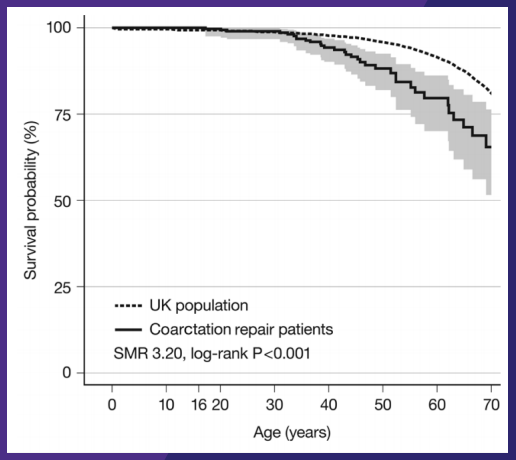


Hager, A. et al (2007). Coarctation Long-term Assessment (COALA): significance of arterial hypertension in a cohort of 404 patients up to 27 years after surgical repair of isolated coarctation of the aorta, even in the absence of restenosis and prosthetic material. *The Journal of Thoracic and Cardiovascular Surgery*, *134*(3), 738-745.

30

Reduced Long Term Survival

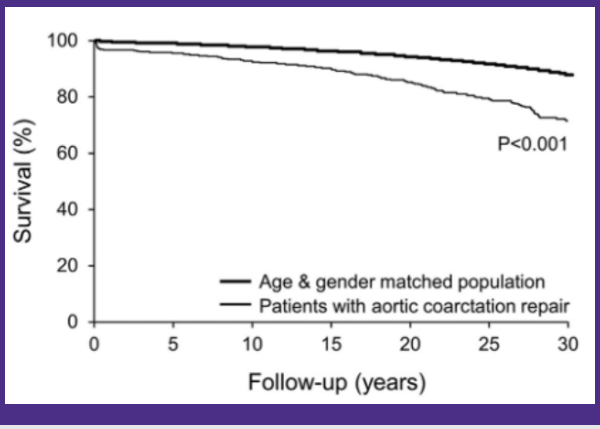
- Reduced long term survival in 834 coarctation of the aorta patient cohort study in the United Kingdom
- Median Age Death 46 years (37-62)
  - Prior VSD or LVOT Obstruction had higher risk of death
- Causes of Death
  - LV failure (10/38)
  - Post-op period for non-coarctation cardiac repairs (5/38)
  - Ruptured descending aorta (2/38)
  - Type A dissection (1/38)
  - Acute Myocardial Infarction (3/38)
  - Sudden Cardiac Death (1/38)
  - Non-cardiac or unknown (14/38)

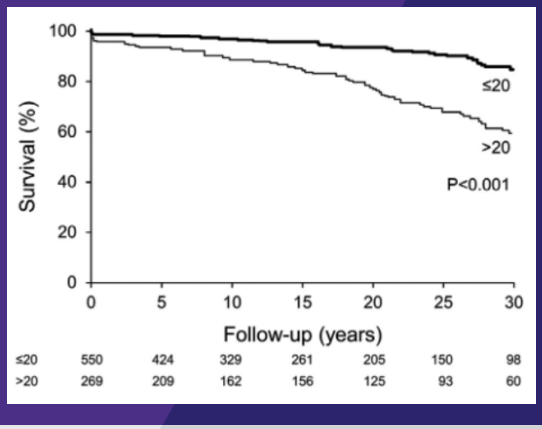


Lee, M. G., et al. (2019). Long-term mortality and cardiovascular burden for adult survivors of coarctation of the aorta. *Heart*, *105*(15), 1190-1196.

31

Lower Survival When Coarctation is Repaired in Adulthood





Brown, M. L. et al. Coarctation of the aorta: lifelong surveillance is mandatory following surgical repair. *Journal of the American College of Cardiology*, *62*(11), 1020-1025.

32

Indications for Intervention

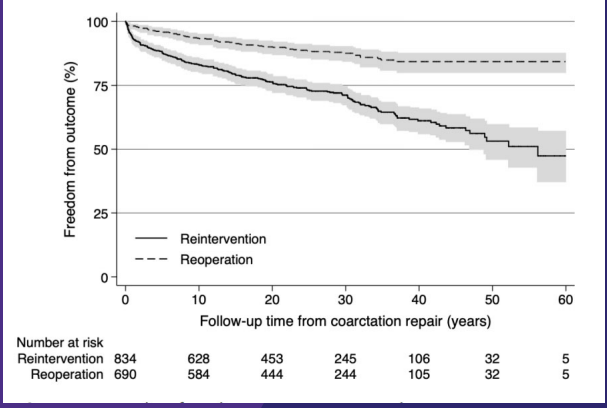
- Upper extremity/lower extremity resting peak-to-peak gradient >20 mm Hg or mean Doppler systolic gradient >20 mm Hg
- Upper extremity/lower extremity gradient >10 mm Hg or mean Doppler gradient >10 mm Hg plus:
  - Decreased LV systolic function
  - Aortic Regurgitation
  - Collateral flow
- >50 % narrowing with hypertension
  - Only in European Guidelines

Stout, K. K., et al. (2019). 2018 AHA/ACC guideline for the management of adults with congenital heart disease: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Journal of the American College of Cardiology*, *73*(12), 1494-1563.
Baumgartner, H. et al. (2020). 2020 ESC Guidelines for the management of adult congenital heart disease. *Eur Heart J*., 00: 1-83.

33

Re-intervention in Common

- Surgical patch repair has higher risk for re-intervention (HR 3.69, CI 2.13-6.37)
- Complications at site of coarctation
  - Aneurysm
  - Psuedoaneurysm
  - Re-coarcation
  - Dissection



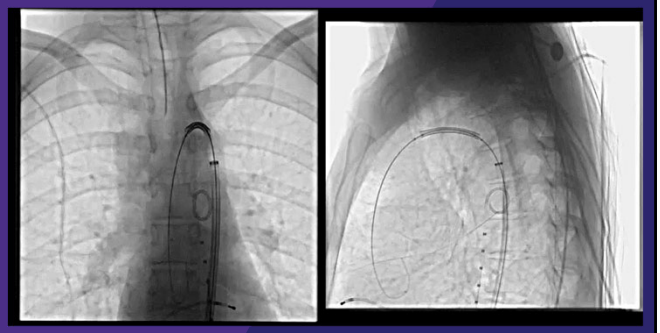
Lee, M. G., et al. (2019). Long-term mortality and cardiovascular burden for adult survivors of coarctation of the aorta. *Heart*, *105*(15), 1190-1196.

34

Stenting has lowest rate of complications at follow-up of 18 months-6 years (median 1.9 years)

Table 7 Intermediate Follow-up Outcomes by Integrated Imaging

	Surgery (n = 16)	Balloon (n = 16)	Stent (n = 56)	p Value (2-Sided)
Any complications*	25.0%	43.8%	12.5%	0.020‡
Aortic wall injury	12.5%	43.8%	7.1%	0.003‡
Dissection/intimal tear	0.0%	6.3%	1.8%	0.598
Aneurysm	12.5%	43.8%	5.4%	<0.001
Coarct:Dao ratio, mean	0.98	0.79	0.80	0.011‡
Coarct:Dao ratio ≥0.6	88%	93%	89%	1.000
Any reobstruction	18.8%	18.8%	14.3%	0.923
Mild†	6.3%	18.8%	12.5%	
Moderate	6.3%	0%	1.8%	
Severe	6.3%	0%	0%	

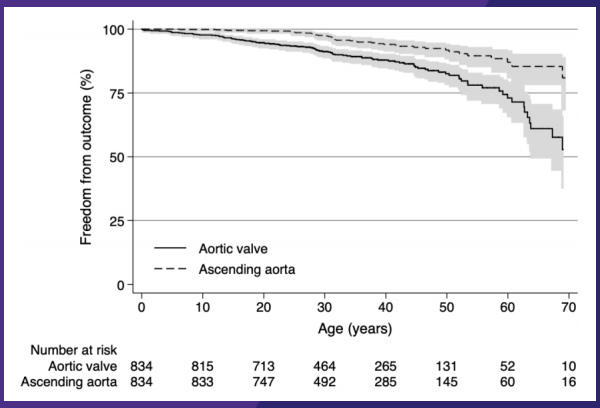


Forbes, T. J. et al. (2011). Comparison of surgical, stent, and balloon angioplasty treatment of native coarctation of the aorta: an observational study by the CCISC (Congenital Cardiovascular Interventional Study Consortium). JACC, *58*(25), 2664-2674.

35

Aortic Valve and Ascending Aortic Interventions are Common

- ~50% of patients have bicuspid aortic valve
- All bicuspid valves should have 4 extremity blood pressures

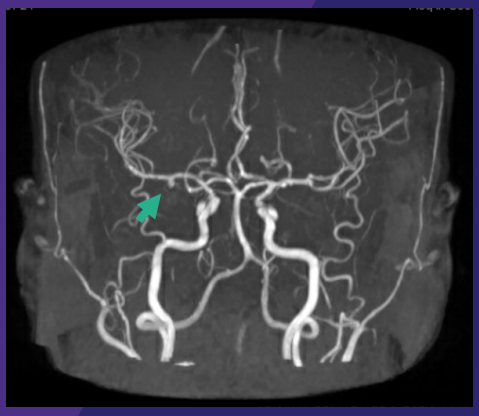


Lee, M. G., et al. (2019). Long-term mortality and cardiovascular burden for adult survivors of coarctation of the aorta. *Heart*, *105*(15), 1190-1196.

36

Intracranial Aneurysms

- Occurs in ~ 10% of Patients
- IIA Recommendation to Screen for Intracranial Aneurysms in 2018 ACHD Guidelines
- Often not seen in young children and teenagers and incidence increased with age
- Often small
- More commonly seen in patients with hypertension
- Unknown if serial screening is indicated



Curtis, S. L. et al. (2012). Results of screening for intracranial aneurysms in patients with coarctation of the aorta. *American journal of neuroradiology*, *33*(6), 1182-1186.
Connolly, H. M., Huston III, J., Brown Jr, R. D., Warnes, C. A., Ammash, N. M., & Tajik, A. J. (2003, December). Intracranial aneurysms in patients with coarctation of the aorta: a prospective magnetic resonance angiographic study of 100 patients. In *Mayo Clinic Proceedings,* 78 (12), 1491-1499
Donti, A. et al. (2015). Frequency of intracranial aneurysms determined by magnetic resonance angiography in children (mean age 16) having operative or endovascular treatment of coarctation of the aorta (mean age 3). *The American journal of cardiology*, *116*(4), 630-633.

37

Patients Require Lifelong Close Cardiology Follow-up

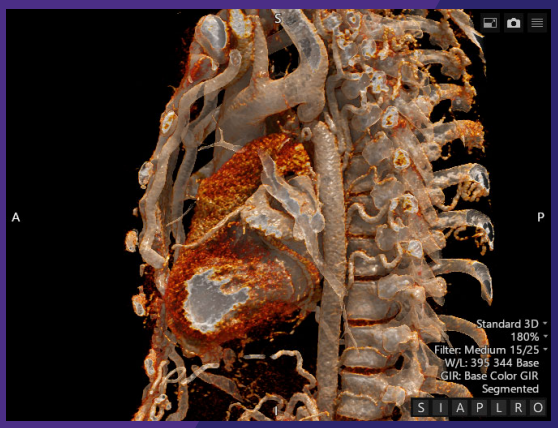
Frequency of Routine Follow-Up and Testing	Physiological Stage A* (mo)	Physiological Stage B* (mo)	Physiological Stage C* (mo)	Physiological Stage D* (mo)
Outpatient ACHD cardiologist	24	24	6-12	3-6
ECG	24	24	12	12
TTE†	24	24	12	12
CMR‡/CCT§	36-60	36-60	12-24	12-24
Exercise test‖	36	24	24	12

Stout, K. K., et al. (2019). 2018 AHA/ACC guideline for the management of adults with congenital heart disease: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Journal of the American College of Cardiology*, *73*(12), 1494-1563.

38

Coarctation of the Aorta Summary

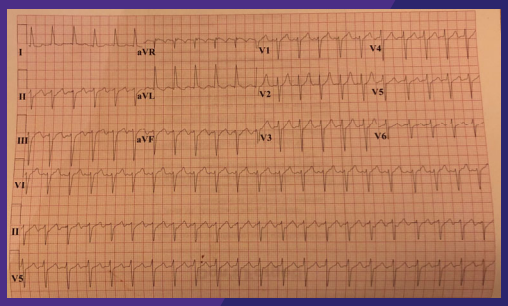
- Hypertension most common symptom
  - Considered as cause of secondary hypertension in patients <30 yr
- Stenting is preferred in adult patients over surgery
- Bicuspid Valve is present in >50% of patients
- All bicuspid valve patients should have 4 extremity blood pressure screening
- Intracranial aneurysms can occur



39

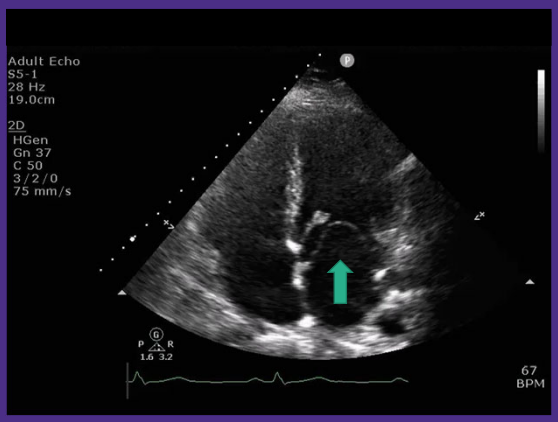
41 year old asymptomatic man at primary care

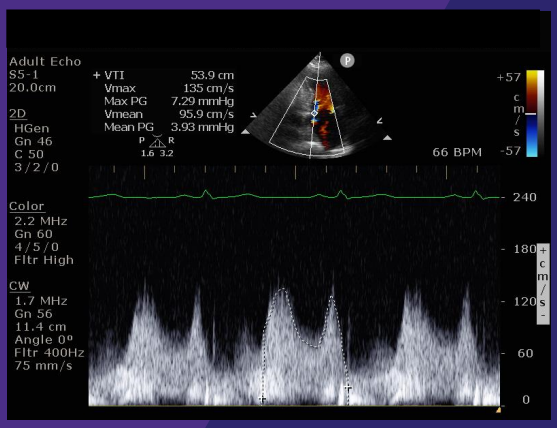
- Vitals with heart rate 147 bpm
- EKG with typical atrial flutter
- Started on diltiazem and apixaban
- Referred to cardiology



40

Echo: Cor Triatrium Sinister



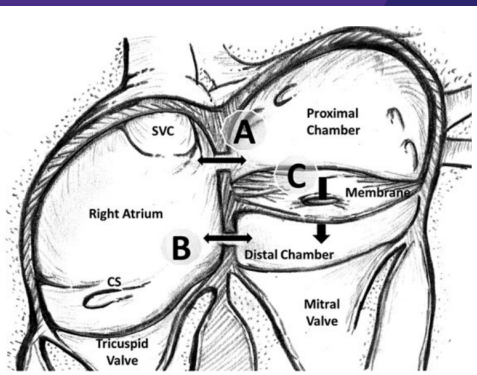


41

Cor Triatrium Sinister

Type of defect	n (%)
Mitral valve regurgitation	42 (24.6)
Atrial septal defect	28 (32.9)
Patent foramen ovale	7 (8.2)
Persistent left superior vena cava	7 (4.1)
Partial anomalous pulmonary venous connection	5 (2.9)
Bicuspid aortic valve	4 (2.3)
Ventricular septal defect	4 (2.3)
Tetralogy of fallot	3 (1.8)
Totally anomalous pulmonary venous connection	2 (1.2)
Left pulmonary vein atresia	2 (1.2)

n, number.



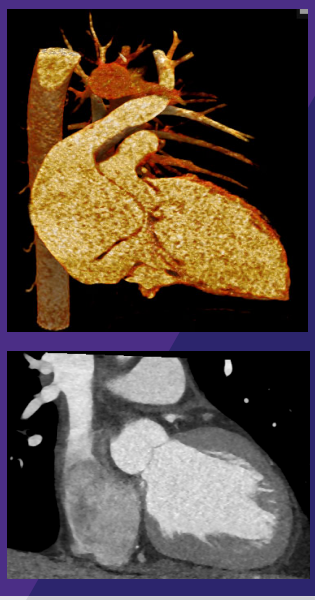
Rudienė, V. et al. (2019). Cor triatriatum sinistrum diagnosed in the adulthood: a systematic review. *Heart*, *105*(15), 1197-1202.

Ozyuksel, A. et al. (2015). Surgical correction of cor triatriatum sinister in the paediatric population: mid-term results in 15 cases. *European Journal of Cardio-Thoracic Surgery*, *47*(1), e25-e28.

42

Cardiac CT Scan

- Evaluation for associated lesions
  - ASD
  - VSD
  - Anomalous pulmonary venous return
- Pulmonary vein stenosis can occur prior to or following surgery



43

Clinical Presentation in Adults

Table 1 Symptoms and clinical findings

Symptoms/clinical findings	All patients (N=171), n (%)	Obstructive membrane (N=70), n (%)	Non-obstructive membrane (N=99), n (%)	P value
Congestive heart failure	46 (26.9)	31 (44.3)	15 (15.2)	<0.001
Pulmonary hypertension	25 (14.6)	19 (27.1)	6 (6.1)	<0.001
Thrombotic/ischaemic events	27 (15.8)	8 (11.4)	19 (19.2)	0.175
Atrial fibrillation	56 (32.8)	25 (35.7)	31 (31.3)	0.549
Syncope	6 (3.5)	2 (2.9)	4 (4.0)	0.999
Pre-syncope	4 (2.3)	1 (1.4)	3 (3.0)	0.643
Chest pain	13 (7.6)	2 (2.9)	11 (11.1)	0.047
Haemorrhage	6 (3.5)	6 (8.6)	0 (0)	0.004
Infections	7 (4.1)	6 (8.6)	1 (1.0)	0.004
Incidental finding	55 (32.2)	6 (8.6)	49 (49.5)	<0.001
Other symptoms	65 (38.0)	37 (52.9)	28 (28.3)	<0.001

n, number.

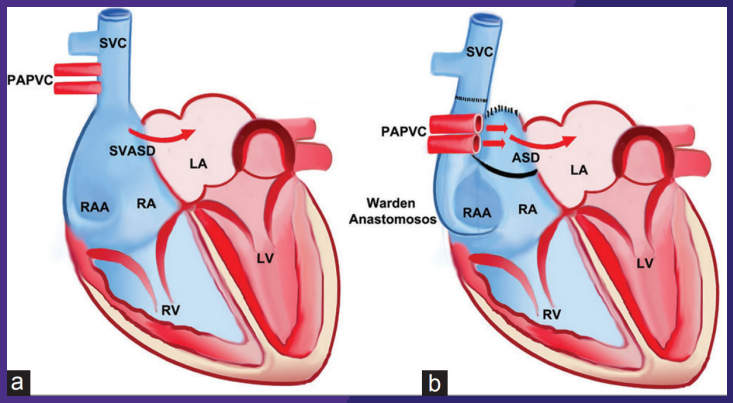
Rudienė, V. et al. (2019). Cor triatriatum sinistrum diagnosed in the adulthood: a systematic review. *Heart, 105*(15), 1197-1202.

44

Treatment

- Atrial flutter ablation
- Surgery
  - Resection of atrial membrane
  - Warden procedure with baffling RPV to the LA via ASD

Warden Procedure

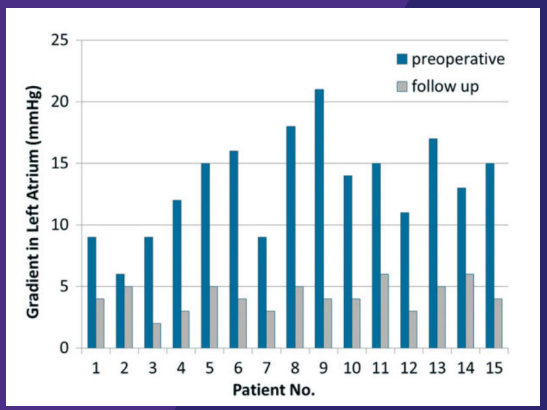


Aggarwal, N. et al. (2016). Warden repair for superior sinus venosus atrial septal defect and anomalous pulmonary venous drainage in children: Anesthesia and transesophageal echocardiography perspectives. *Annals of cardiac anaesthesia*, *19*(2), 293.

45

Follow-up

- Re-obstruction is rare
- Pulmonary vein stenosis can occur prior to or following surgery

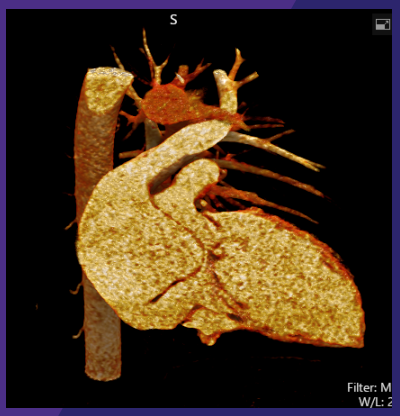


Ozyuksel, A. et al. (2015). Surgical correction of cor triatriatum sinister in the paediatric population: mid-term results in 15 cases. *European Journal of Cardio-Thoracic Surgery*, *47*(1), e25-e28.

46

Cor Triatrium Sinister Summary

- Membrane creating obstruction in the left atrium
- Associated with other congenital heart defects
- Re-obstruction rare after surgery
- Most common complications
  - Heart failure
  - Pulmonary hypertension
  - Thrombotic / ischemic events
  - Atrial fibrillation



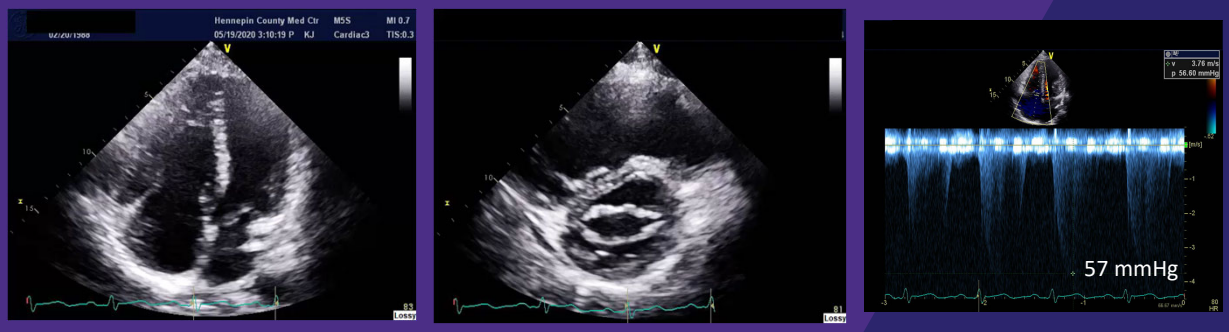
47

32 year old at primary care for pre-operative clearance for an orbital tumor

- Murmur heart on exam
- Noted to have worsening exercise tolerance
- Surgery was delayed for cardiac evaluation

48

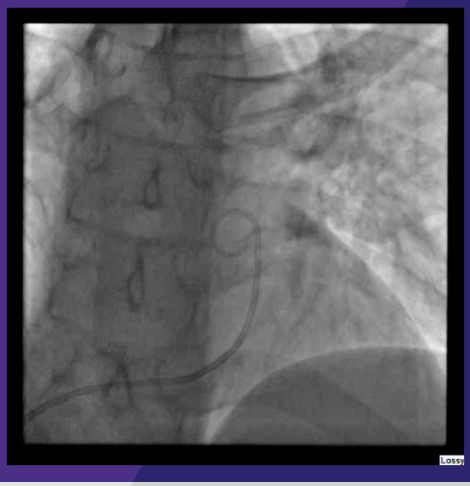
Echo – Diagnosed with Pulmonary Hypertension



49

Right Heart Catheterization

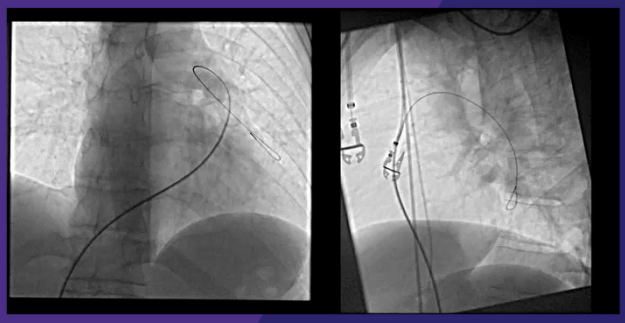
- Elevated RV pressures but normal pulmonary artery pressures
  - Mean RA 5 mmHg
  - RV 83/0 mmHg
  - PA 29/7 mmHg; mean 16 mm Hg
  - PCWP 8 mmHg



50

Branch Pulmonary Artery Stenosis

- Decision to intervene based upon
  - RV hypertension
  - Progressive RV enlargement / decreasing function
  - Distribution of pulmonary blood flow
- Restenosis is common
  - 46% in a series of 26 patients at mean follow-up of 41 months

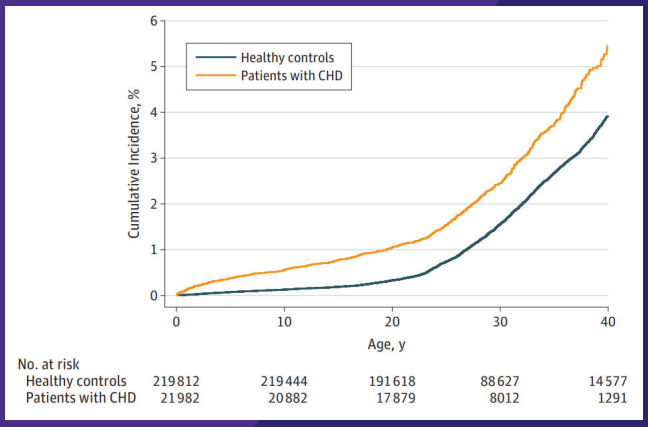


Gonzalez, I. et al. (2013). Medium and long-term outcomes after bilateral pulmonary artery stenting in children and adults with congenital heart disease. *Pediatric cardiology*, *34*(1), 179-184.

51

Cancer and Congenital Heart Disease

- Swedish cohort study 21,982 patients with CHD up to age 41 years
- Hazard ration of 2.24 (95% CI 2.01-2.48) for developing any type of malignancy
- Similar results found in cohort studies in Taiwan, Canada, and California

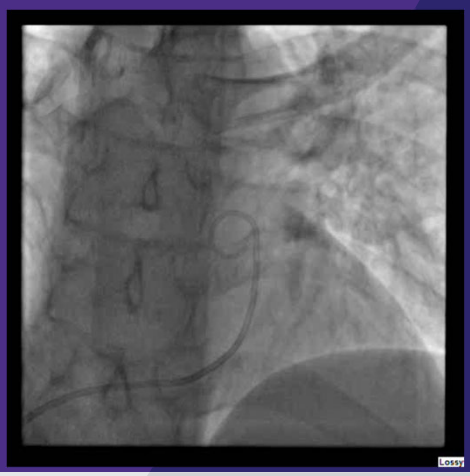


Mandalenakis, Z., et al. (2019). Risk of cancer among children and young adults with congenital heart disease compared with healthy controls. *JAMA network open*, *2*(7), e196762-e196762.
Collins, R. T. et al. (2018). Congenital heart disease complexity and childhood cancer risk. *Birth Defects Research*, *110*(17), 1314-1321.
Gurvitz, M., et al. (2016). Prevalence of cancer in adults with congenital heart disease compared with the general population. *The American Journal of Cardiology*, *118*(11), 1742-1750.
Lee, Y. S., et al. (2015). The risk of cancer in patients with congenital heart disease: a nationwide population-based cohort study in Taiwan. *PLoS One*, *10*(2), e0116844.

52

Branch Pulmonary Artery Stenosis Stenting Summary

- Rare cause of RV hypertension
- Intervention is based on symptoms and RV function / dilation
- Restenosis is common following intervention
- All patients need lifelong follow-up



HOPE DISCOVERED HERE | Minneapolis Heart Institute Foundation

53

36 year old woman with chest pain during exercise

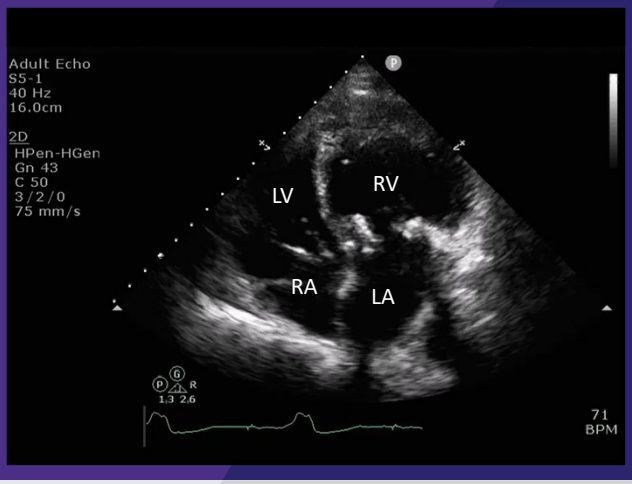
- 15 years: Syncope, no significant evaluation
- 28 years: murmur and told she likely had mitral valve prolapse
- 20s: Active, but felt she had poor exercise endurance
- 36 years: Chest tightness while training for a triathlon
  - Exercise EKG stress test, peak HR 156 bpm, peak BP 124/60
  - Consistent with an “MI”
  - Recommended outpatient echo

HOPE DISCOVERED HERE | Minneapolis Heart Institute Foundation

54

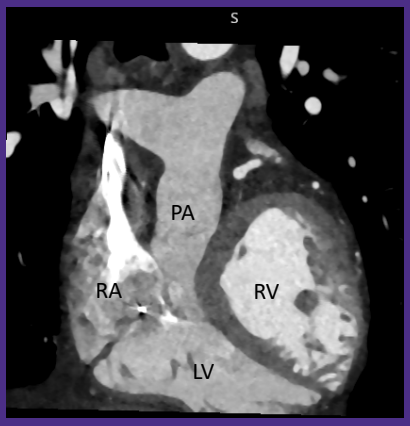
Echocardiogram

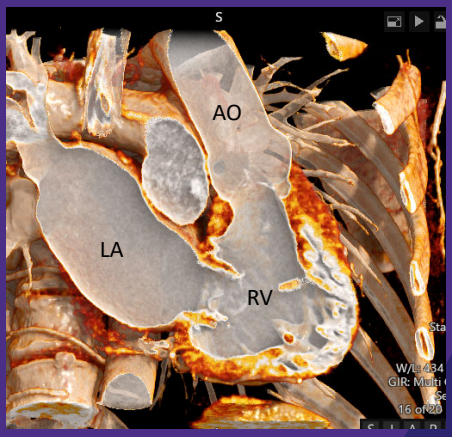
- Congenitally corrected transposition of the great arteries
- Systemic right ventricle
  - Moderately reduced EF
- Epstein like tricuspid valve

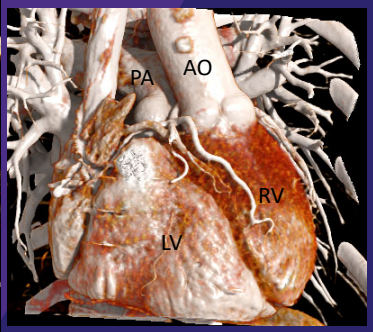


55

Congenitally Corrected Transposition of the Great Arteries



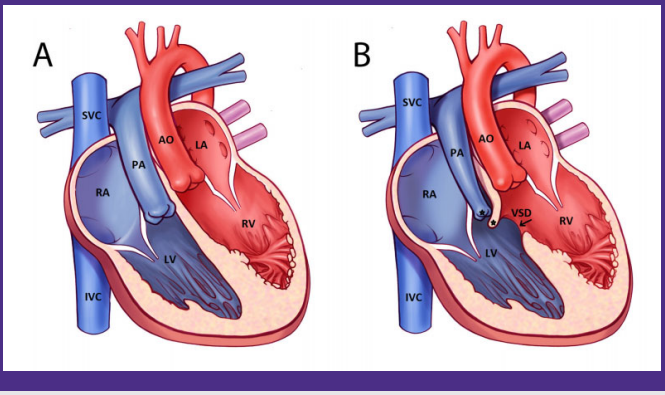


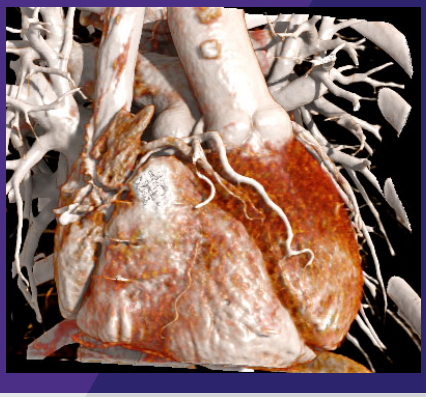


56

Congenitally Corrected Transposition of the Great Arteries

- Abnormal L looping of the primitive heart tube



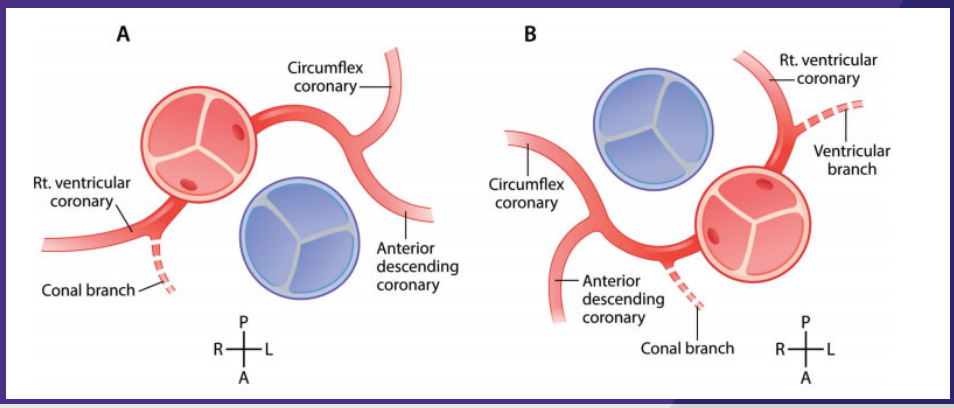


Kutty, S., et al. (2018). Contemporary management and outcomes in congenitally corrected transposition of the great arteries. *Heart*, *104*(14), 1148-1155.

57

Coronary Arteries are a Mirror Image of Normal Anatomy

Normal Anatomy **ccTGA**

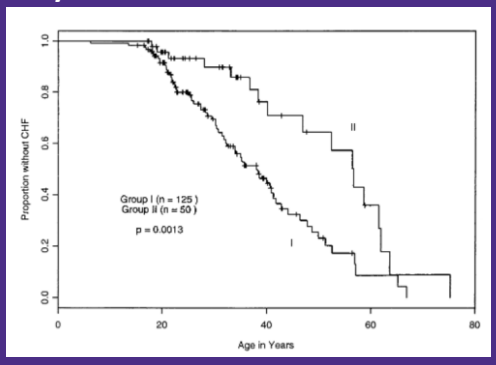


Kutty, S., et al. (2018). Contemporary management and outcomes in congenitally corrected transposition of the great arteries. *Heart*, *104*(14), 1148-1155.

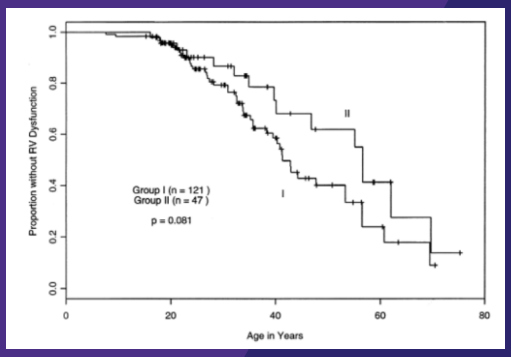
58

Heart Failure is Common During Adulthood

Any Heart Failure



Moderate to Severe RV Dysfunction



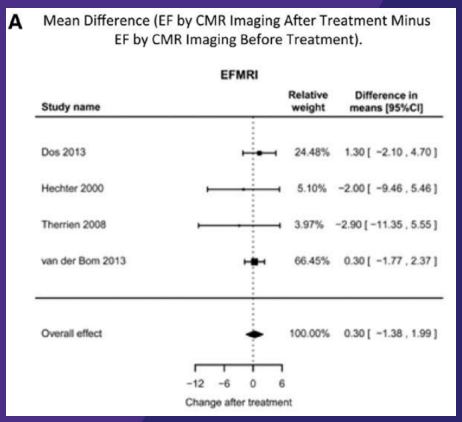
Group I: Patients with associated cardiac abnormalities
Group II: Isolated ccTGA

Graham, T. P. et al. (2000). Long-term outcome in congenitally corrected transposition of the great arteries: a multi-institutional study. *Journal of the American College of Cardiology*, *36*(1), 255-261.

59

Medical Treatment for Heart Failure is Controversial

- Systematic review failed to show benefit with conventional HF therapy
  - Underpowered (total of 187 patients)
  - Included both D and L Transposition of the Great Arteries
  - Up to 50% drop out rates
  - Inclusion criteria included near normal RV EF
  - Follow-up times as short as 4 months



Stout, K. K. et al. (2019). 2018 AHA/ACC guideline for the management of adults with congenital heart disease: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Journal of the American College of Cardiology*, *73*(12), 1494-1563.

60

Follow-up

- 37 years: Started on Ace-I for EF 45%, follow-up systemic RV EF 53%
- 39 -43years: Developed arrhythmias: Asymptomatic NSVT, atrial flutter, and Mobitz type II AV block
- 43 years: Complete AV block, received dual chamber pacemaker

61

Rhythm Abnormalities Common

- Pacemakers common
  - 45% patients with ccTGA and associated abnormalities
  - 27% patients with isolated ccTGA
- Arrhythmias
  - 47% patients with ccTGA and associated abnormalities
  - 29% patients with isolated ccTGA
- Sudden Cardiac Death
  - 5 of 39 patient had sudden cardiac death in a single center series
    - All had normal to mildly reduced RV function
    - NYHA Class I-II symptoms

Mongeon, F. P. et al. (2011). Congenitally corrected transposition of the great arteries: ventricular function at the time of systemic atrioventricular valve replacement predicts long-term ventricular function. *Journal of the American College of Cardiology*, *57*(20), 2008-2017.

McCombe, A. et al. (2016). Sudden cardiac death in adults with congenitally corrected transposition of the great arteries. *Open Heart*, *3*(2).

62

Follow-up

- 44 years: Moderate to severe TV valve regurgitation and moderate systemic RV dysfunction (EF mid 40s)
  - Received 27mm Mosaic porcine bioprosthetic systemic AV valve
  - Early endocarditis at 6 days post-operatively
- 45 years: 6 months post TV valve replacement, developed increased resting gradient 16-20mmHg with thickened leaflets that resolved with warfarin

HOPE DISCOVERED HERE | Minneapolis Heart Institute Foundation

63

Tricuspid Regurgitation is Common

Table 4. Demographic and Clinical Variables by Patient Group

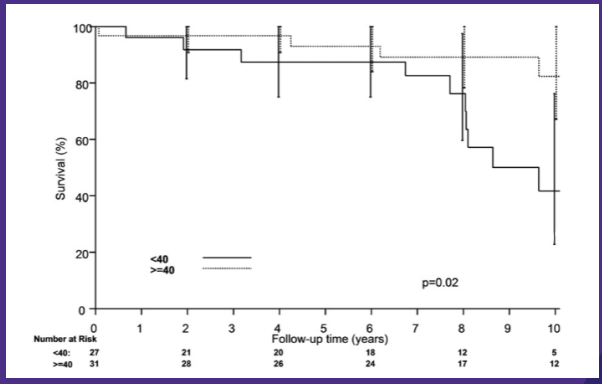
	Group I (Associated Lesions) (n = 132)	Group II (No Associated Lesions) (n = 50)	p Value
Age (yr, mean ± SD)	32 ± 12	34 ± 15	NS
Gender	37% female	52% female	NS
CHF	51%	34%	0.04
RV Dysfunction:			
Any	70%	55%	NS
Moderate or severe	39%	32%	NS
TR:			
Any	82%	85%	NS
Moderate or severe	57%	40%	NS

Graham, T. P. et al. (2000). Long-term outcome in congenitally corrected transposition of the great arteries: a multi-institutional study. *Journal of the American College of Cardiology*, *36*(1), 255-261.

HOPE DISCOVERED HERE | Minneapolis Heart Institute Foundation

64

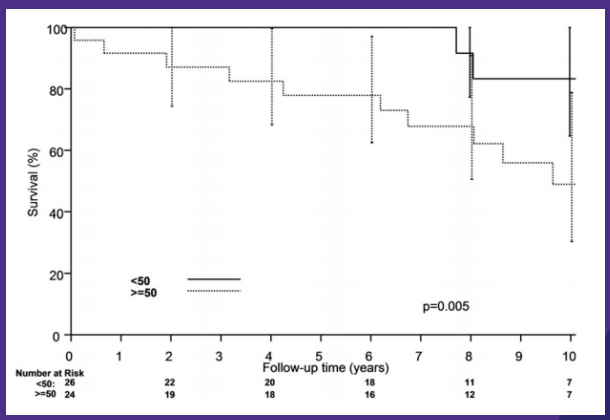
Survival is poor following surgery after systemic RV EF <40%



Mongeon, F. P. et al. (2011). Congenitally corrected transposition of the great arteries: ventricular function at the time of systemic atrioventricular valve replacement predicts long-term ventricular function. *Journal of the American College of Cardiology*, *57*(20), 2008-2017.

65

Survival Poor if Sub-Pulmonary Pressure >50mmHg

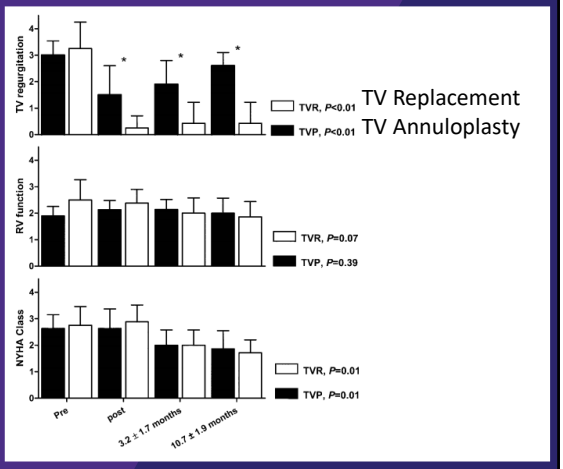


Mongeon, F. P. et al. (2011). Congenitally corrected transposition of the great arteries: ventricular function at the time of systemic atrioventricular valve replacement predicts long-term ventricular function. *Journal of the American College of Cardiology*, *57*(20), 2008-2017.

66

Tricuspid Valve Replacement is Favored Over Repair

- High rates of TV regurgitation following repair compared to replacement
  - Series was small (16 patients)
- Tricuspid valve typically dysplastic or Epstein like



Scherptong, R. W. et al. (2009). Tricuspid Valve Surgery in Adults With a Dysfunctional Systemic Right Ventricle. *Circulation*, *119*(11), 1467.

67

ccTGA Patients Require Close Long Term Follow-up

- Monitor for
  - Heart Failure
  - Arrhythmias
  - Systemic Tricuspid Regurgitation

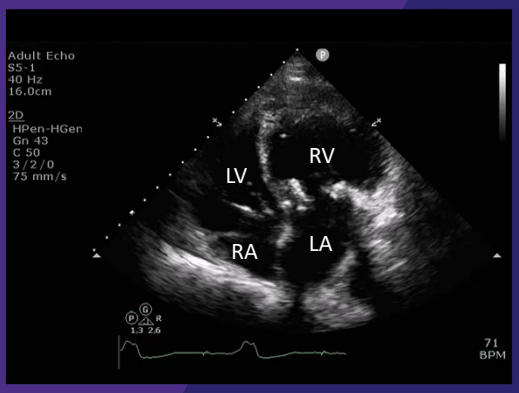
TABLE 31 CCTGA: Routine Follow-Up and Testing Intervals

Frequency of Routine Follow-Up and Testing	Physiological Stage A* (mo)	Physiological Stage B* (mo)	Physiological Stage C* (mo)	Physiological Stage D* (mo)
Outpatient ACHD cardiologist	12	12	6-12	3-6
ECG	12	12	12	12
TTE†	12-24	12	12	12
Pulse oximetry	As needed	As needed	Each visit	Each visit
Holter monitor	12-60	12-60	12-36	12
CMR‡/CCT§	36-60	36-60	12-24	12
Exercise test‖	36-60	36-60	12-24	12

68

Congenitally Corrected Transposition of the Great Arteries

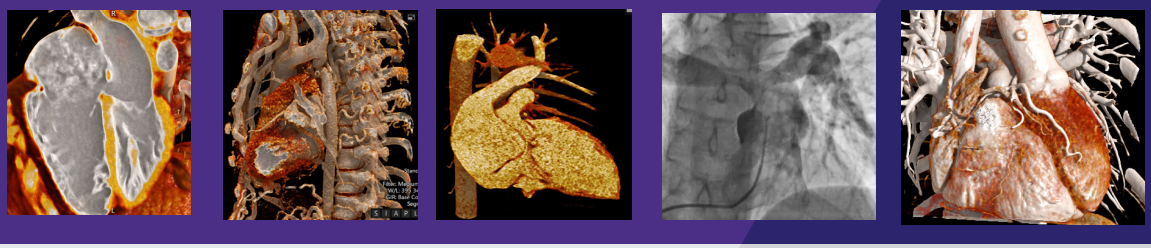
- Most common complex CHD to present in adulthood
- Heart failure is almost universal in adulthood
- Arrhythmias are common
- Tricuspid valve regurgitation extremely common
  - Correction recommended prior to LV EF <40%



69

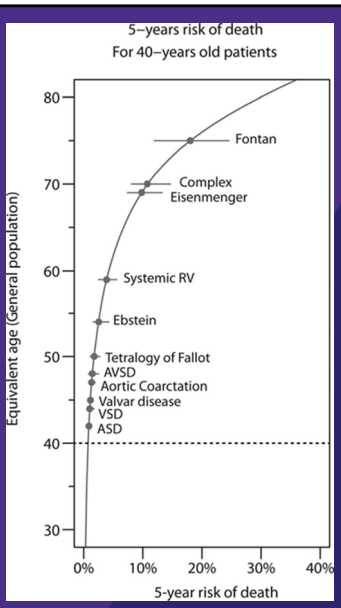
Conclusion

- Congenital Heart Disease Can Present in Adulthood
  - Often diagnosed by echocardiogram
- First presentation in adulthood is often either atrial arrhythmias or heart failure in a young patient



70

CHD Patients Have Increased Mortality Compared to the General Population



Newberger. Trends in CHD, the next decade. Circulation 2016

71

Recurrence of CHD in Offspring

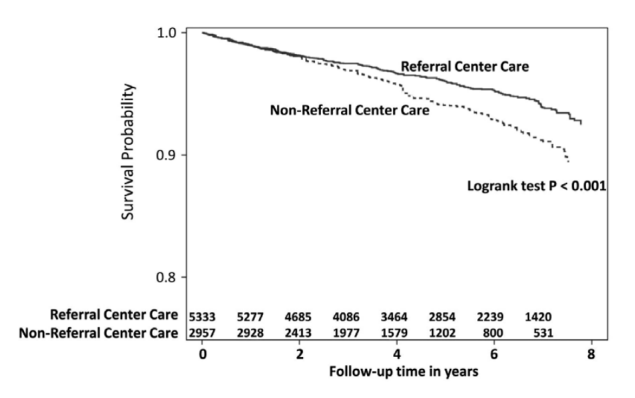
- Prenatal screening with fetal echocardiography can be offered to women to screen for CHD if either parent has a history of CHD
- Same lesions do not always occur

	Recurrence rate (%)*	
	Women	Men
ASD	4–6	1.5–3.5
VSD	6–10	2–3.5
AVSD	11.5–14	1–4.5
PDA	3.5–4	2–2.5
CoA	4–6.5	2–3.5
Marfan/HTAD	50[b]	
LVOTO	8–18	3–4
RVOTO (PS)	4–6.5	2–3.5
Eisenmenger syndrome	6	NR
TOF	2–2.5	1.5
Pulmonary atresia/VSD	NR	NR
TGA	2[b]	
ccTGA	3–5[b]	
UVH (HLHS)	21[b]	

Baumgartner, H. et al. (2020). 2020 ESC Guidelines for the management of adult congenital heart disease. *Eur Heart J.*, 00: 1-83.

72

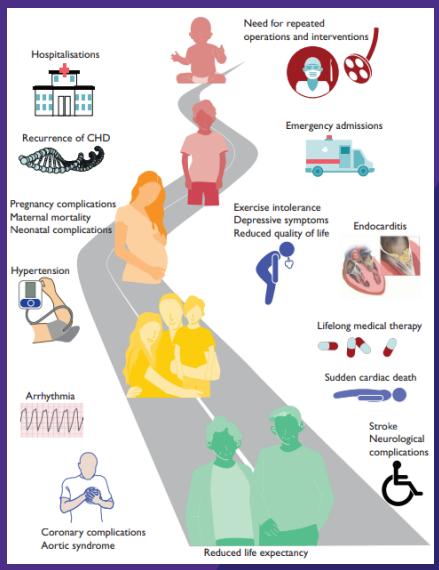
Improved Outcomes When Cared For At a Comprehensive Adult Congenital Program



Mylotte, D., Pilote, L., Ionescu-Ittu, R., Abrahamowicz, M., Khairy, P., Therrien, J., ... & Marelli, A. (2014). Specialized adult congenital heart disease care: the impact of policy on mortality. *Circulation*, *129*(18), 1804-1812.

73

CHD: A Life Long Condition



Baumgartner, H. et al. (2020). 2020 ESC Guidelines for the management of adult congenital heart disease. *Eur Heart J.*, 00: 1-83.

74