Pulmonary Hypertension Associated with Congenital Heart Disease

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Disclosure

- Honoraria - Actelion
- Research grants form Actelion

The Nice Classification (2013)

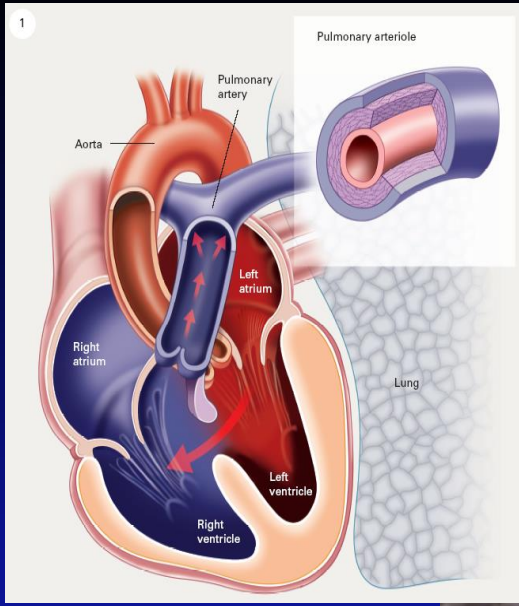
1. Pulmonary arterial hypertension
2. Pulmonary hypertension due to left heart disease
3. Pulmonary hypertension due to lung diseases and/or hypoxia
4. Chronic tromboembolic pulmonary hypertension
5. Pulmonary hypertension with unclear multifactorial mechanisms

PAH
1.1 Idiopathic PAH
1.2 Heritable PAH
1.3 Drug and toxin induced
1.4 Associated PAH

Associated PAH
1.4.1. Connective tissue disease
1.4.2. HIV infection
1.4.3. Portal hypertension
1.4.4. Congenital heart disease
1.4.5. Schistosomiasis

PAH-CHD
1. Eisenmenger syndrome
2. Left-to-right shunts
3. Small defects
4. Post-operative PAH

Blok et al. Expert Rev. Cardiovasc. Ther. 2015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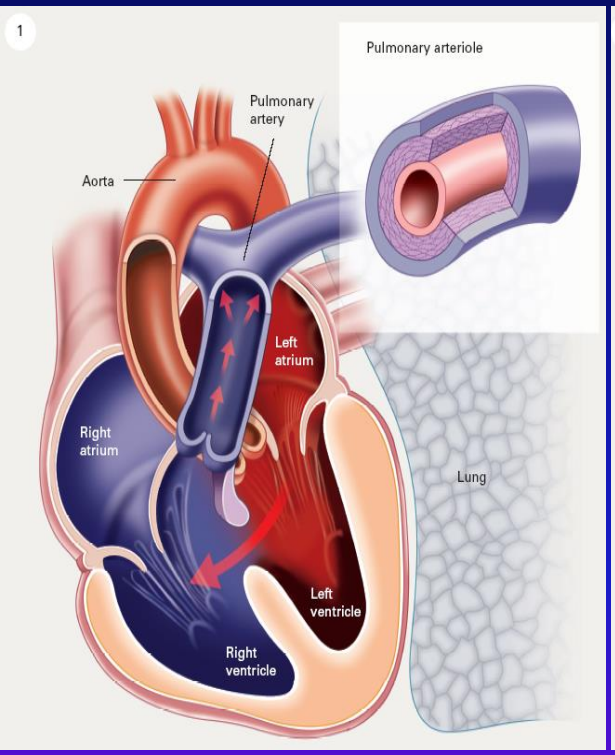
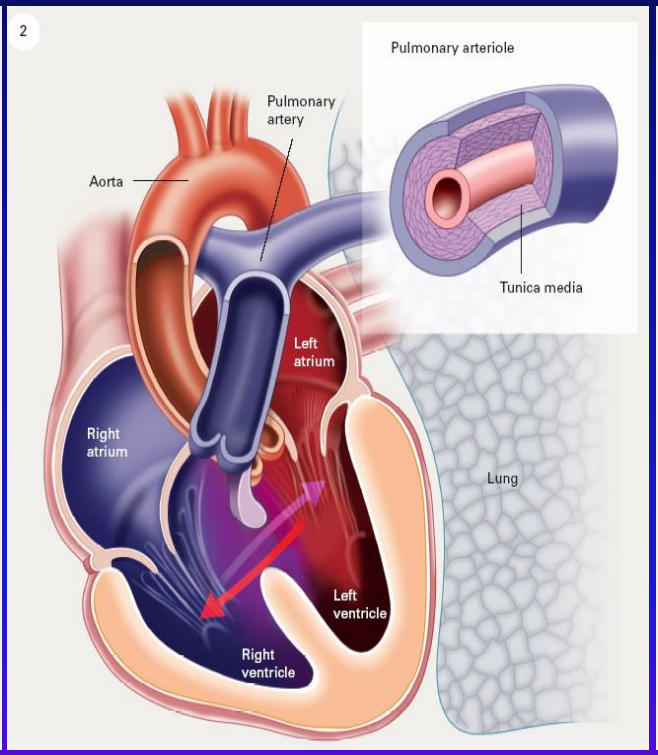
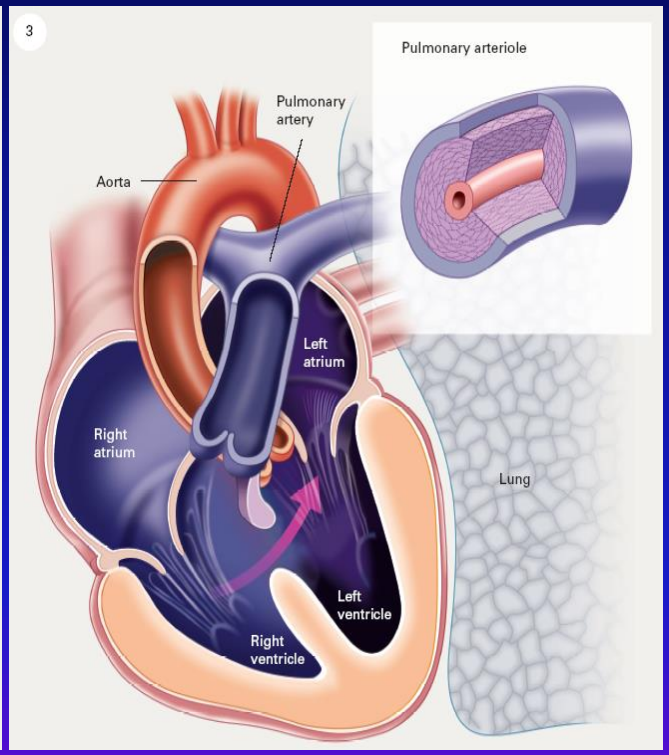
Pulmonary arteriole
Pulmonary artery
Aorta
Left atrium
Right atrium
Lung
Left ventricle
Right ventricle

Evolution of Eisenmenger Syndrome







ASD, VSD or complex defect increases pulmonary blood flow via left-to-right shunt

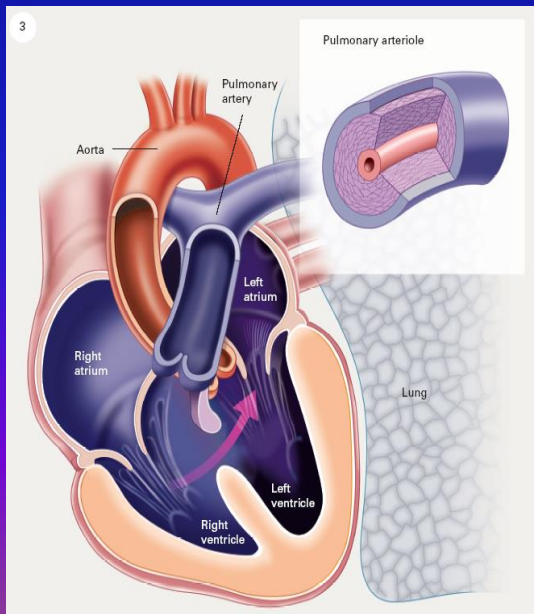
Pulmonary resistance rises and results in bi-directional flow

Reversal of shunt: right-to-left →

Eisenmenger syndrome

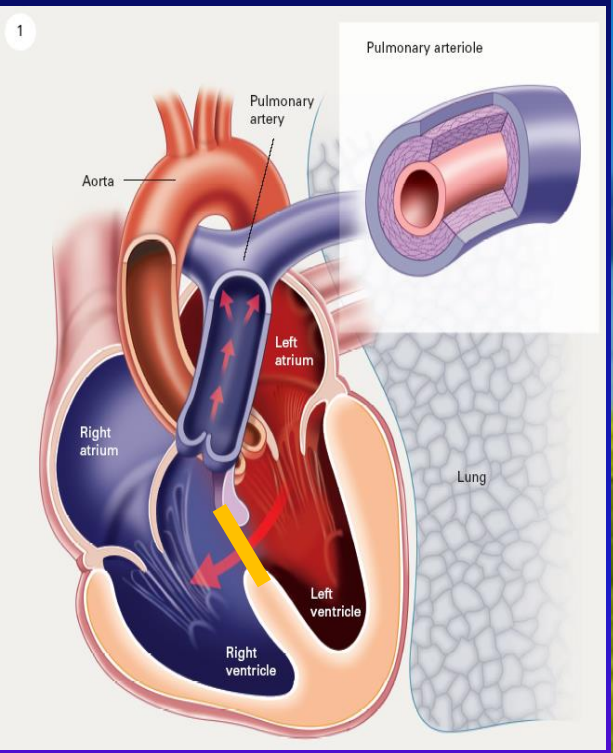
Eisenmenger physiology

- Cyanosis rather than a drop in CO
- Shunting through the cardiac defect
  - Significant hypoxia
  - Increasing ventilation/perfusion (V/Q) mismatch
  - Exercise intolerance



Dimopoulos et al. Current Opinion in Cardiology 2008, 23:545

How to prevent the pulmonary vascular disease



ASD, VSD or complex defect increases pulmonary blood flow via left-to-right shunt

Cardiac Septal Defects

- What to close?
- When to close?
- When not to close?

When to Close a VSD?

- Large VSDs (Qp/Qs > 2:1)
- Close before age 12 months

Moss and Adams, Pediatric Cardiology Textbook, 2013

European Heart Journal
doi:10.1093/eurheartj/ehv317

ESC/ERS GUIDELINES

2015 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension

The Joint Task Force for the Diagnosis and Treatment of Pulmonary Hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS)

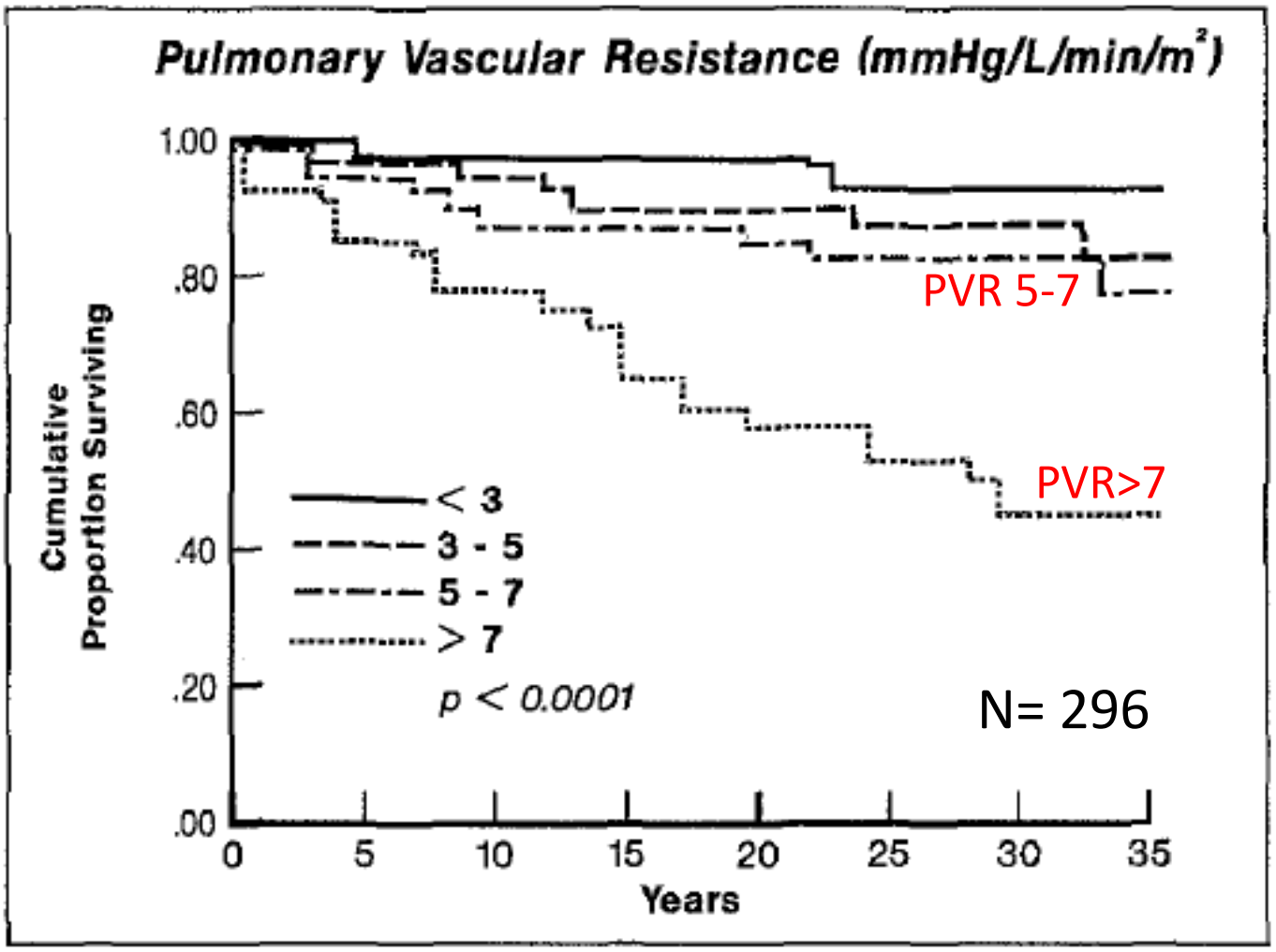
To Close or not to Close?
Pulmonary Vascular Resistance

Recommendations			Class[a]	Level[b]
PVRi (WU • m^2)	PVR (WU)	Correctable[d]		
<4	<2.3	Yes	IIa	C
>8	>4.6	No	IIa	C
4–8	2.3–4.6	Individual patient evaluation in tertiary centres	IIa	C

European Society of Cardiology 2015 Guidelines

Survival by Pulmonary Vascular Resistance before VSD Closure

Surgery
1954-1960



Moller et al. Am J Cardiol 1991

Does It Work?

A young women with VSD repaired "on time"

- 21 year old lady born with coarctation and VSD
- Coarctation repair age 18 days
- CHF – VSD closure age 9 months
- PAH – Echo at 14 years TR gradient 65 mmHg
- No F/U since 14 years of age

Pulmonary Hypertension and Pregnancy

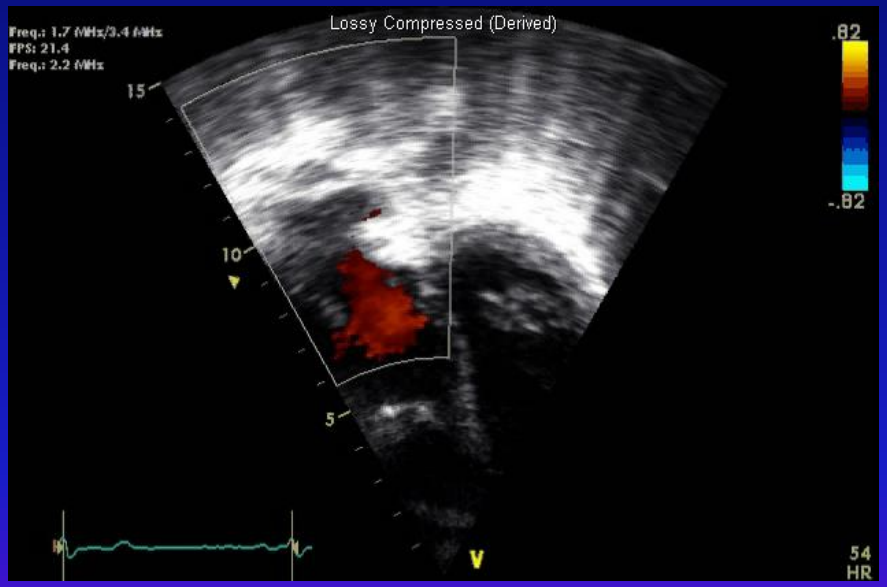
- Presented at 8 w gestation
- Echo – suspected pulmonary hypertension (very faint TR signal)
- No shunt
- Cath (9 w gest.)
  - PAP 92/42, mean 56 mmHg
  - PVR 12.7, PVR/SVR 0.7

Pulmonary Hypertension and Pregnancy

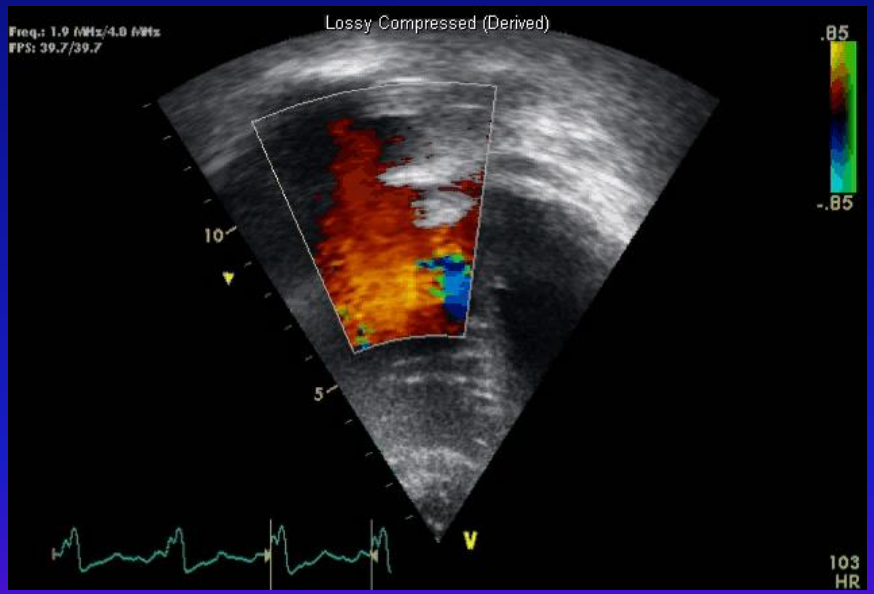
- Strongly advised against continuation of the pregnancy (28%-36% mortality) – Elected to continue
- Rx – Sildenafil
- Elective C/S at 34 weeks
- 1750 gr baby boy
- Bosentan added post partum

Pulmonary Hypertension and Pregnancy

8 w gestation



7 days post partum
Sildenafil



TR gradient 90 mmHg

Pulmonary Hypertension in Adults with Repaired Septal Defects

- 12 % of 896 patients with ASD
- 13% of 710 patients with VSD

Engelfriet et al. Heart 2007

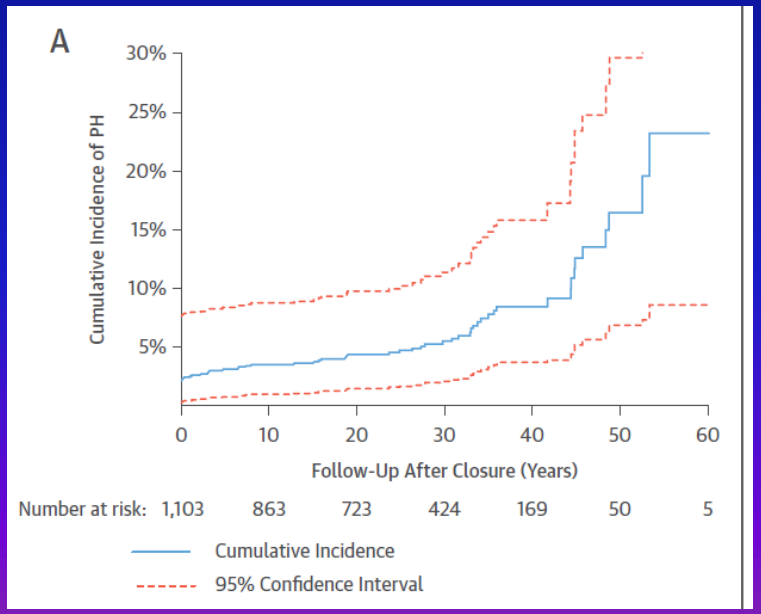
Pulmonary Hypertension in Adults with Repaired Septal Defects

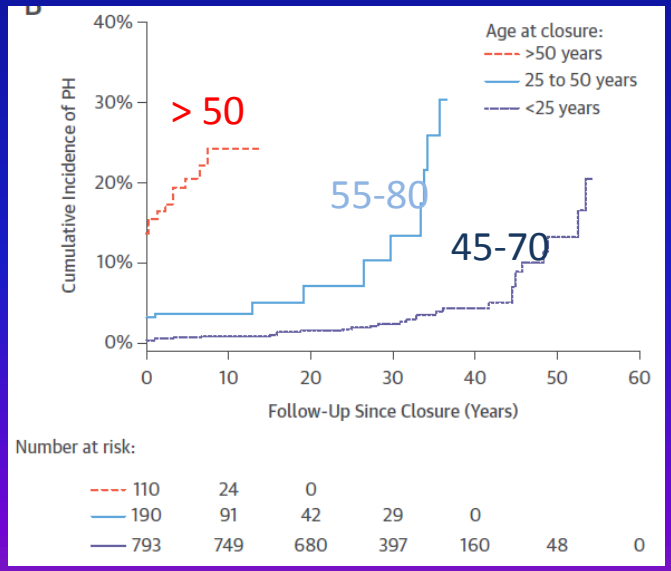
- 1103 shunt patients
- Closure performed
  - Interquartile range 1977 to 1990, median 1987
- Median age 8.5 y (interquartile range: 2.9 - 27.6)
  - VSD 283
  - ASD 382
  - Primum ASD 92
- LV disease excluded

van Riel et a. JACC 2015

Pulmonary Hypertension in Adults with Repaired Septal Defects

- Cumulative incidence of PH
  - Immediately after closure 2.1%
  - After 50 years >15%
  - ASD closed <25 years - 4.3% developed PAH





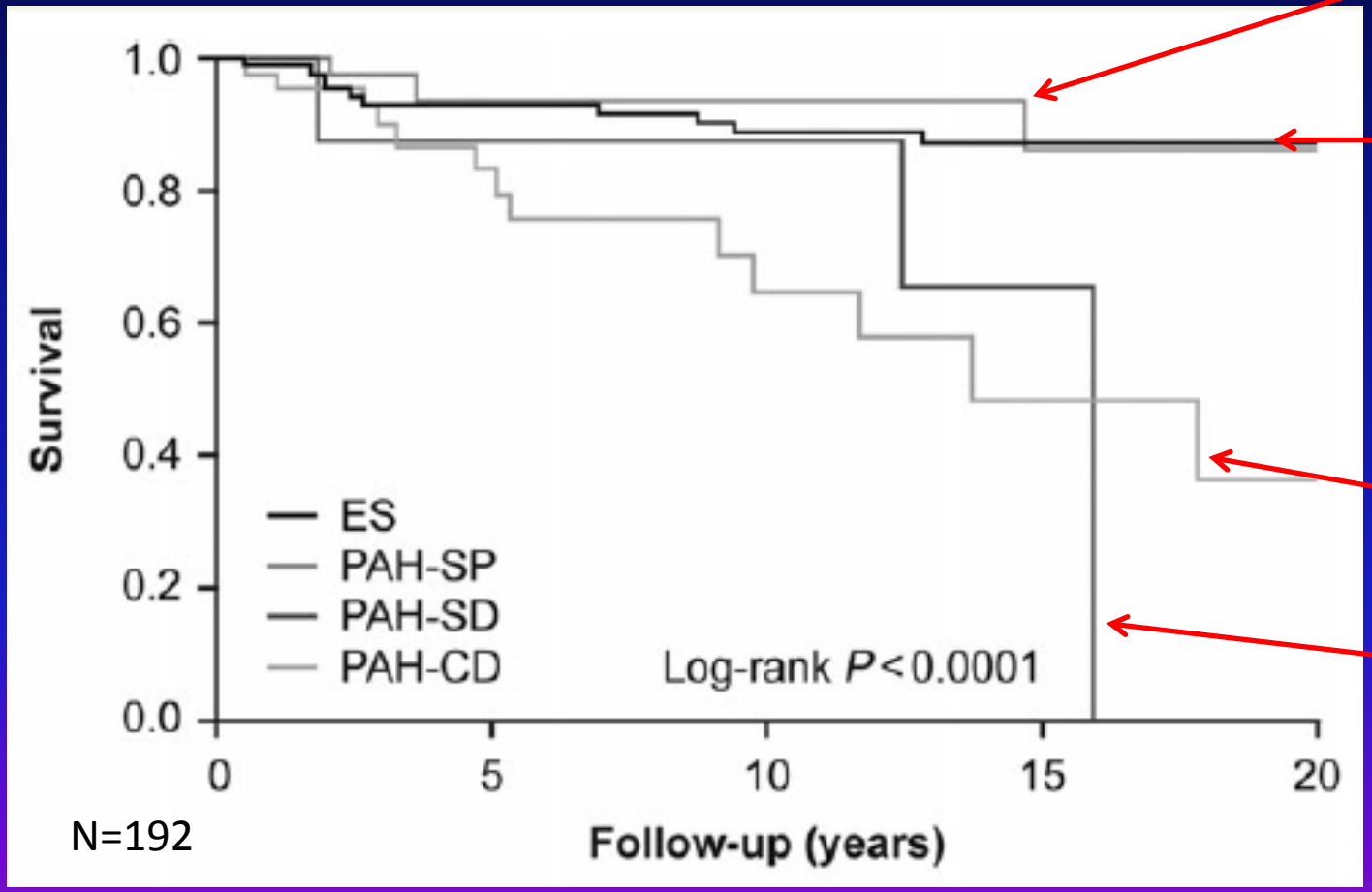
van Riel et a. JACC 2015

Repaired septal defects

Need for F/U even when all looks good

van Riel et a. JACC 2015

Survival of CHD-PAH



L to R shunt
age 47y, N=48

Eisenmenger
Age 41y, N=90

Corrected
Age 36y, N=44

Small defects
Age 25y, N=10

Manes et al. Eu HJ 2014

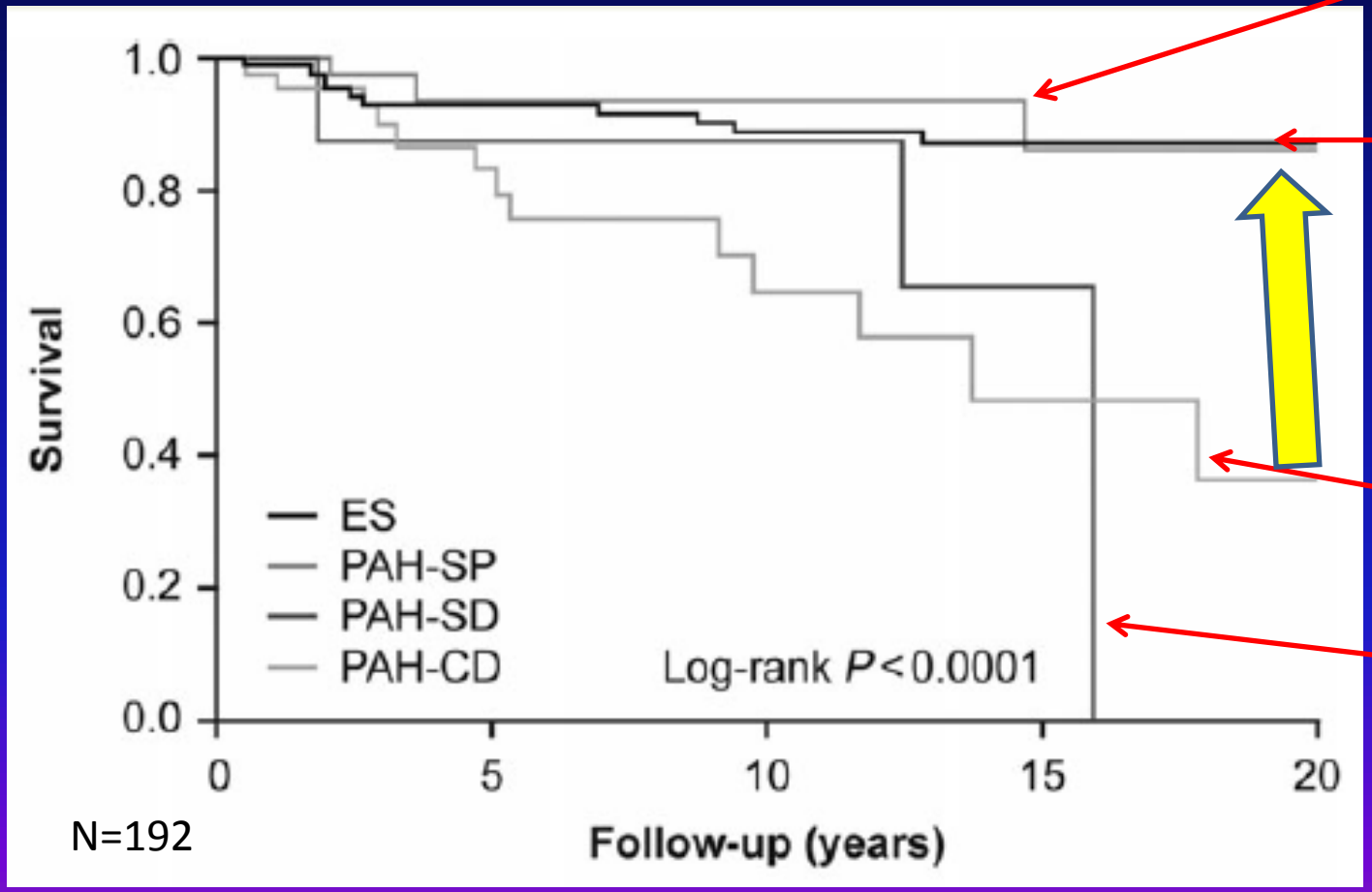
PAH Survival
Congenital HD Vs Idiopathic

- Five-year survival
- PAH-CHD (n=192) 91%
- Idiopathic PAH (n=278) 63%

Single center, same treatment strategy

Manes et al. Eu HJ 2014

Suboptimal Criteria for Operability



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Manes et al. Eu HJ 2014

Treatment

PAH Drugs in Children and Adults with CHD

- Limited data
- Mostly small studies and registries
- Safety and tolerability – established

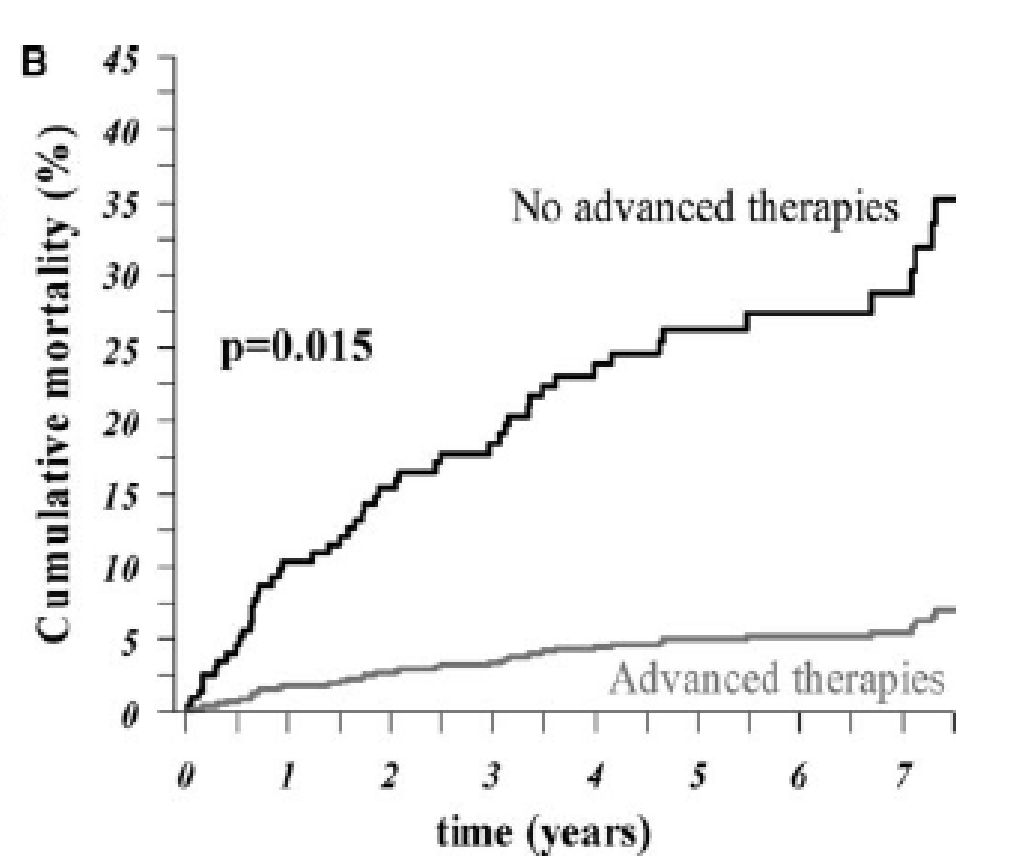
- Since vascular disease mechanism similar to IPAH – same drugs may have similar effects

- Calcium channel blockers are not used in Eisenmenger syndrome due to the risk of systemic vasodilation

PAH Drugs in Children and Adults with CHD

- Improve
  - Survival or time to clinical worsening
  - Hemodynamics
  - Quality of life
  - Exercise capacity

Eisenmenger Syndrome Survival Improvement



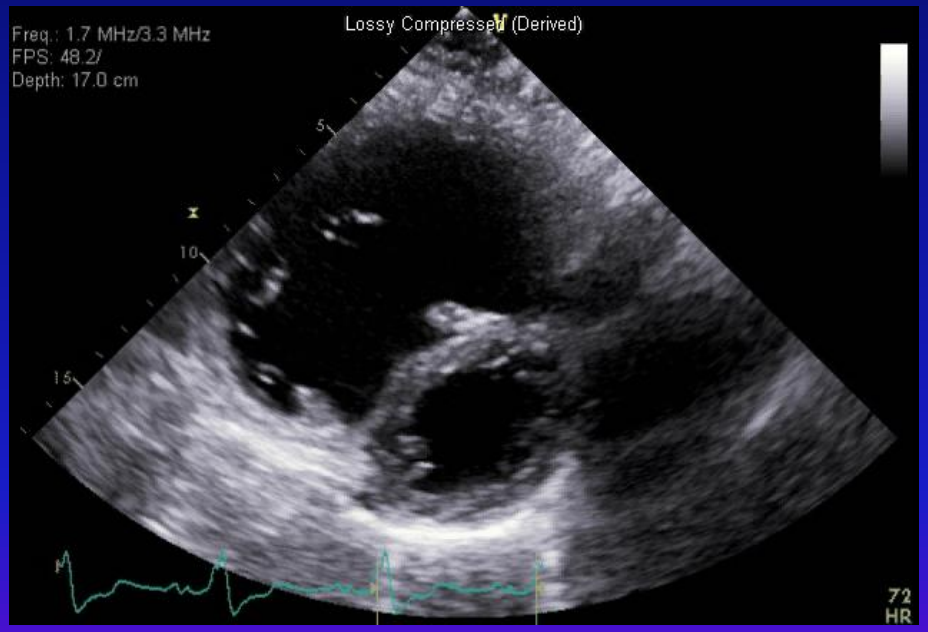
229 patients
age 34.5 y

Dimopoulos et al. Circ 2010

Septal Defect Closure In Adults

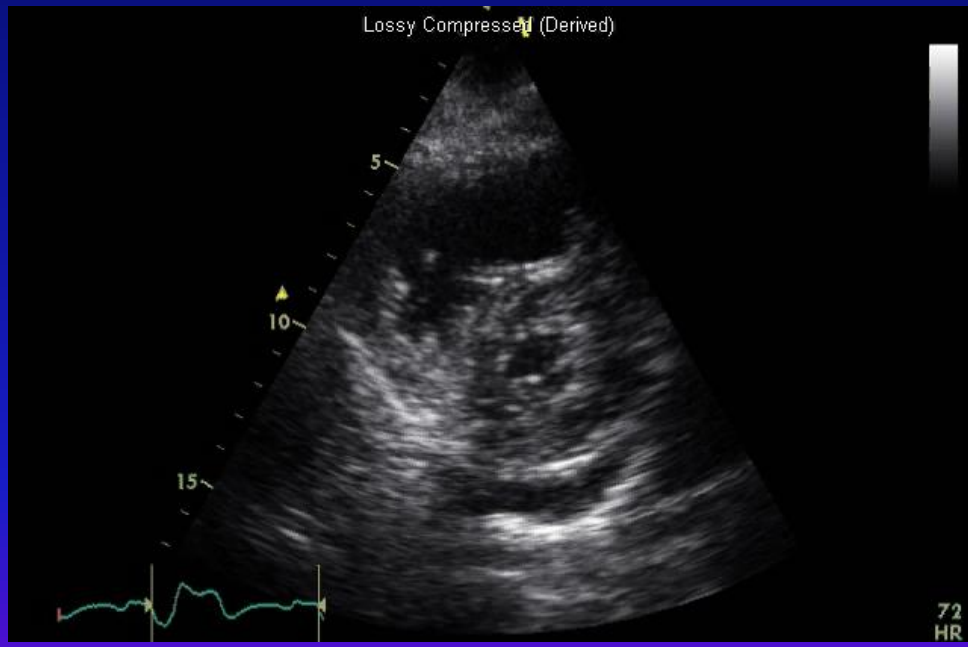
ASD Closure in Adult
61 year old lady

Pre closure



TR 60 mmHg

Post closure



TR 29 mmHg

Most studies show clinical improvement with ASD closure

Treat and Repair

- Adults with elevated PVR
- Treatment with PAH therapies for months
- Repair

- Promising short term results
- ASD Kijima et al. *Circ J* Nov 2015
- VSD Hu et al. *J Thorac Dis* 2015

Summary

- Early closure of septal defect is beneficial in most but not all patients
- Patients with septal defects may develop pulmonary vascular disease even if repaired “on time”
- Pulmonary Hypertension may develop late – long term follow up is needed
- Patients with PAH-CHD respond to pulmonary vasodilators
- Late closure of the defect may be beneficial in selected patients