Pulmonary Hypertension Associated with Congenital Heart Disease

Amiram Nir
Hadassah, Jerusalem
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

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 $\rightarrow$ 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

How to prevent the pulmonary vascular disease

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 \(\rightarrow\) Eisenmenger syndrome
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
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

<table>
<thead>
<tr>
<th>PVRi (WU • m²)</th>
<th>PVR (WU)</th>
<th>Correctable</th>
<th>Class</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;4</td>
<td>&lt;2.3</td>
<td>Yes</td>
<td>IIa</td>
<td>C</td>
</tr>
<tr>
<td>&gt;8</td>
<td>&gt;4.6</td>
<td>No</td>
<td>IIa</td>
<td>C</td>
</tr>
<tr>
<td>4–8</td>
<td>2.3–4.6</td>
<td>Individual patient evaluation in tertiary centres</td>
<td>IIa</td>
<td>C</td>
</tr>
</tbody>
</table>
Survival by Pulmonary Vascular Resistance before VSD Closure

PVR 5-7

PVR > 7

N = 296

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 al. JACC 2015
Repaired septal defects

Need for F/U even when all looks good

van Riel et a. JACC 2015
Survival of CHD-PAH

N=192

Small defects
Age 25y, N=10

Eisenmenger
Age 41y, N=90

Corrected
Age 36y, N=44

L to R shunt
Age 47y, N=48

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

- Small defects: Age 25y, N=10
- Eisenmenger: Age 41y, N=90
- Corrected: Age 36y, N=44
- L to R shunt: Age 47y, N=48

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

Post closure

TR 60 mmHg

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
- 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