Should We Revisit Our Thinking About Eisenmenger Syndrome?

Gary Webb
San Francisco
March 2011

Overview

- Definition and causes
- Eisenmenger mortality
  - Historic
  - Recent
- Impact of “advanced therapy”
- Evidence of favorable remodelling
  - Medication
  - PA banding

Eisenmenger Definition

- Large communication between systemic and pulmonary circuits
- Initially large L-R shunt
- Progressive rise in PVR
- Pulmonary flow falls, R-L shunt predominates

Definition of Eisenmenger

1. Oximetry < 90% on room air in absence of pulmonary AV malformation
2. Large enough defect (ASD ≥ 20mm; VSD ≥ 10mm; PDA ≥ 4mm)
3. Hemodynamics
   - Mean PAP ≥ 40 mmHg
   - Mean wedge/LA < 15 mmHg
   - PVR > 10 Wood units/m²
   - Qp/Qs < 1.0
4. Absence of other potential causes of PHT

Fernandes AJC 91:632: 2003
Causes of Eisenmenger

- Simple shunts
  - ASD
  - VSD
  - PDA
- Large AP shunts
  - AP collaterals
  - Surgical shunts
- Complex lesions
  - AVSD
  - TGA/VSD
  - ccTGA/VSD
  - Truncus

Eisenmenger at a Glance

- High PVR usually established by 2 years
- Fairly healthy childhood
- Slowly progressive cyanosis
- Exercise limitation ∝ degree of hypoxemia
- A progressive, dynamic condition that will worsen

Eisenmenger Mortality

<table>
<thead>
<tr>
<th>Oxygen Saturation (%)</th>
<th>Predicted Htgb (g/dL)</th>
<th>95% CI (g/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>16.3</td>
<td>14.4–17.3</td>
</tr>
<tr>
<td>15</td>
<td>17.8</td>
<td>16.0–19.5</td>
</tr>
<tr>
<td>20</td>
<td>18.8</td>
<td>17.0–20.1</td>
</tr>
<tr>
<td>25</td>
<td>19.7</td>
<td>18.4–21.0</td>
</tr>
<tr>
<td>30</td>
<td>20.6</td>
<td>19.1–22.3</td>
</tr>
<tr>
<td>35</td>
<td>21.9</td>
<td>20.4–23.4</td>
</tr>
<tr>
<td>40</td>
<td>23.2</td>
<td>21.6–24.9</td>
</tr>
<tr>
<td>45</td>
<td>24.3</td>
<td>22.1–26.1</td>
</tr>
<tr>
<td>50</td>
<td>26.0</td>
<td>24.0–27.9</td>
</tr>
</tbody>
</table>

CL: confidence interval.

UCLA Eisenmenger Study

- 77 Eisenmenger adults (retrospective)
- Group A = 47 VSD
- Group B = 14 truncus
- Group C = 16 univentricular
  - (comparable age ranges & means)
- Followed 4.4 years (5 to 15)
**UCLA Eisenmenger Study**

- Group A: VSD
- Group B: Truncus
- Group C: UniV

<table>
<thead>
<tr>
<th>Living at start</th>
<th>Died</th>
<th>Age at death (mean)</th>
<th>Survivors' age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group A</td>
<td>47</td>
<td>45</td>
<td>37</td>
</tr>
<tr>
<td>Group B</td>
<td>14</td>
<td>4</td>
<td>31</td>
</tr>
<tr>
<td>Group C</td>
<td>16</td>
<td>4</td>
<td>33</td>
</tr>
</tbody>
</table>

Survivors' age: 37 years

**Toronto Eisenmenger Study**

- 109 ES patients
- Followed mean 6.3 years
- 33 deaths
- 9 transplants
- Predictors - atrial flutter/fib and poor NYHA class

**Toronto Eisenmenger Study**

- 109 Eisenmenger adults (retrospective)
- Simple = 66 (43 VSD, 13 ASD, 10 PDA)
- Complex = 43 (AVSD, TA, UniV, TGA)
- Mean age = 29 ± 11 yrs
- Followed 6.3 years (1 to 40)

**Toronto Eisenmenger Study**

- 109 Eisenmenger adults
- 33 (30%) died in 6.3 years mean f/u – mean age 37 years
- 7 deaths (22%) were sudden
- 14 deaths (44%) in CHF

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**UCLA Eisenmenger Study**

- 77 Eisenmenger adults
- 27 (35%) died in 4.4 years mean f/u
- 17 deaths (63%) were sudden

**Toronto Eisenmenger Study**

- 109 Eisenmenger adults
- Followed mean 6.3 years
- 33 deaths
- Predictors: atrial flutter/fib and poor NYHA class
Toronto Eisenmenger Study

- 109 Eisenmenger adults
- 9 (8%) transplanted in 6.3 years mean f/u
  mean age 37 years
- 7 lung Tx, 2 HLT
- 4 died during study

Cantor, Harrison et al AJC 1999

Toronto Eisenmenger Deaths

Unpublished

Survival – PPH vs. ES

<table>
<thead>
<tr>
<th></th>
<th>PPH</th>
<th>Eisenmenger</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 year</td>
<td>77%</td>
<td>97%</td>
</tr>
<tr>
<td>2 years</td>
<td>69%</td>
<td>89%</td>
</tr>
<tr>
<td>3 years</td>
<td>35%</td>
<td>77%</td>
</tr>
</tbody>
</table>

Impact of Advanced Therapy

Improved Survival Among Patients With Eisenmenger Syndrome Receiving Advanced Therapy for Primary Arterial Hypertension

Dimopoulos Circulation 2010
### Reversal of Pulmonary Hypertension and Subsequent Repair of Atrial Septal Defect After Treatment With Continuous Intravenous Epoprostenol

Adriano F. Rest, MD, Miguel A. Quitmann, MD, William A. Zoghbi, MD, and George F. Nocera, MD

We report the first case in the world literature of a patient with an atrial septal defect, severe pulmonary hypertension, and reciprocating pulmonary and systemic pressures who underwent a successful closure of an ASD following prolonged therapy with the potent, nonselective prostacyclin derivatives of continuous intravenous epoprostenol in apparently inoperable patients with congenital heart disease can be associated with significant survival of pulmonary hypertension, and outcomes in an expandable ring. J Heart Lung Transplant 2005;24:901-9. Copyright © 2005 by the International Society for Heart and Lung Transplantation.

Schwerzmann UC 2005

### Pulmonary Artery Banding

- Batista paper
- "Successful reversal of pulmonary hypertension in Eisenmenger complex"
- *Arq Bras Cardiol* 68;279-80:1997


Schwerzmann UC 2005
Pulmonary Artery Banding

• Lancet 1997 “Batista strikes again to tackle Eisenmenger complex” 349:1605

Pulmonary Artery Banding

• Banding of the pulmonary artery in children with ventricular septal defects and pulmonary hypertension. A preliminary report.


Pulmonary Artery Banding

• Reversibility of plexogenic pulmonary arteriopathy following banding of the pulmonary artery.

Wagenvoort CA, Wagenvoort N, Draulans-Noë Y.

Pulmonary Artery Banding

• In 28 patients with congenital heart disease with a shunt and pulmonary hypertension, lung biopsy specimens were taken during a banding procedure of the pulmonary artery; then, in the same patients, lung tissue became available during correction of the cardiac defect some years later.

Pulmonary Artery Banding

• Medial hypertrophy appeared to have a prominent tendency to regression. With intimal lesions, regression depended to a large extent on the type of lesion. Intimal thickening based on longitudinal smooth muscle tissue was almost completely reversible. Post-thrombotic intimal fibrosis was also potentially reversible. In plexogenic pulmonary arteriopathy, the earlier lesions, particularly cellular intimal proliferation, showed regression.

Pulmonary Artery Banding

• Concentric-laminar intimal fibrosis regressed as long as it was mild, that is, occluding less than one fifth of the average arterial lumen. If more severe, there was no tendency to regression and often it even progressed. Changes like fibrinoid necrosis and plexiform lesions are ominous because of their tendency to progression.
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Supplemental Oxygen

- Prevailing wisdom - "supplementary O2 will not benefit the cyanotic patient with a cardiac R-L shunt"
- Not true

Supplemental Oxygen

<table>
<thead>
<tr>
<th></th>
<th>paO2</th>
<th>saturation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Room air</td>
<td>53</td>
<td>87%</td>
</tr>
<tr>
<td>Nasal oxygen 3L/min.</td>
<td>73</td>
<td>93%</td>
</tr>
<tr>
<td>FiO2 100%</td>
<td>190</td>
<td>98%</td>
</tr>
</tbody>
</table>

Acute effects of 40% oxygen supplementation in adults with cyanotic congenital heart disease

F Walker, M J Mullen, S J Woods, G D Wells

Walker, Heart 2004
Figure 3: Change in systemic arterial oxygen saturation (SaO2) with administration of 40% and 100% oxygen (Naf). Walker, Heart 2004