Chronic Thromboembolic Pulmonary Hypertension

Nick H. Kim, M.D.

Associate Clinical Professor of Medicine
Pulmonary and Critical Care Medicine
Director, Fellowship Program
Director, Pulmonary Vascular Program
University of California, San Diego
Disclosures

- Research Support: Actelion, Gilead, United Therapeutics

- Consultancy: Bayer
Natural History of Chronic Thromboembolic Pulmonary Hypertension

ACUTE PE

Genetic / Intrinsic Variables
Prothrombotic Tendencies
Recurrent TE Events

Resolution without Hemodynamic Compromise

96-99%
Natural History of Chronic Thromboembolic Pulmonary Hypertension

- ACUTE PE
- Genetic / Intrinsic Variables
- Prothrombotic Tendencies
- Recurrent TE Events
- Small Vessel Changes
- CTEPH
Clinical Classification of Pulmonary Hypertension (Dana Point 2008)

1. PAH
   - Idiopathic PAH
   - Heritable
   - Drug- and toxin-induced
   - Persistent PH of newborn
   - Associated with:
     - CTD
     - HIV infection
     - portal hypertension
     - CHD
     - schistosomiasis
     - chronic hemolytic anemia

1’. PVOD and PCH

2. PH Due to Left Heart Disease
   - Systolic dysfunction
   - Diastolic dysfunction
   - Valvular disease

3. PH Due to Lung Diseases and / or Hypoxia
   - COPD
   - ILD
   - Other pulmonary diseases with mixed restrictive and obstructive pattern
   - Sleep-disordered breathing
   - Alveolar hypoventilation disorders
   - Chronic exposure to high altitude
   - Developmental abnormalities

4. CTEPH

5. PH With Unclear Multifactorial Mechanisms
   - Hematologic disorders
   - Systemic disorders
   - Metabolic disorders
   - Others

VQ Scan: Screening Test of Choice
Retrospective: compared with DSA
- Of 78 CTEPH pts confirmed by DSA:
  - VQ: 75 high, 1 intermediate, 2 low
  - CTPA: 40 positive, 38 negative
- VQ: sens 96-97%, spec 90-95%
- CTPA: sens 51%, spec 99%
Pitfalls with CTPA:
(Under-Dx CTEPH, Over-Dx PAH?)

**PAH-QuERI**: PAH dx’d without VQ = 43%

CTPA: CTE disease?
VQ Scan (same patient)
CTEPH: Multi-Slice CTA

CTEPH: MR Angiogram
CTEPH: Angioscopy
What’s Impressive?
CTEPH: Experience Matters

Thorough Endarterectomy

Jamieson Type III Disease
Not Always Just A PTE

Other Surgical Procedures

<table>
<thead>
<tr>
<th>Year</th>
<th>CABG</th>
<th>Valve</th>
<th>PFO/ASD</th>
</tr>
</thead>
<tbody>
<tr>
<td>2009</td>
<td>12.2</td>
<td>3.2</td>
<td>16.1</td>
</tr>
<tr>
<td>2010</td>
<td>5.7</td>
<td>4.1</td>
<td>20.5</td>
</tr>
<tr>
<td>2011</td>
<td>7.3</td>
<td>1.6</td>
<td>20.2</td>
</tr>
<tr>
<td>2012</td>
<td>6.3</td>
<td>5.4</td>
<td>15.3</td>
</tr>
</tbody>
</table>
Perioperative Mortality Rates: UCSD

Slides courtesy of: W. Auger
CTEPH Registry - Operability

- All patients: 679
- Operable: 427
- Non-operable: 252

- Operated: 386
- Non-operated: 293
- Operated: 373
- Non-operated: 54
- Operated: 13
- Non-operated: 239
Mortality – Center Expertise

Wilcoxon 2-sample test

PEA per year

- In-hospital death
- 1 y. death

<table>
<thead>
<tr>
<th>Category</th>
<th>In-hospital Death</th>
<th>1 y. Death</th>
</tr>
</thead>
<tbody>
<tr>
<td>all (17 c.)</td>
<td>4.7%</td>
<td>7%</td>
</tr>
<tr>
<td>n=1-10 (6 c.)</td>
<td>7.4%</td>
<td>11.1%</td>
</tr>
<tr>
<td>n=11-50 (8 c.)</td>
<td>4.7%</td>
<td>7.3%</td>
</tr>
<tr>
<td>n&gt;50 (3 c.)</td>
<td>3.5%</td>
<td>5%</td>
</tr>
</tbody>
</table>

AATS Toronto, May 2010
International Scientific & Educational Workshop
in CTEPH

27th & 28th June 2011
Robinson College, Cambridge, UK
CTEPH (blue) vs PAH (green)

Pubmed results

YEAR

# of Articles

Total: 3,640

Total: 651
CTEPH: Hot Topics

- Operability Criteria
- Access/number of PEA Centers
- Role of Medical Therapy
CTEPH and Operability Assessment

1) Is there chronic thromboembolic disease?

2) What is the PVR?

3) How experienced is your surgeon?

4) How experienced is your pre/post-operative team?
Preoperative Evaluation

• Is there CTE (proximal) disease?
  ▪ VQ scan / PA angio / angioscopy
  CT angio / MRA / PA ultrasound

• Is there microvascular (inoperable) disease?
  ▪ Hemodynamic to radiographic discrepancy / Expert opinion
CTEPH: Preoperative PVR

Operative mortality %

Pulmonary resistance dynes·s·cm⁻⁵
Of 22 deaths (4.4%):

- 17 (77%) had residual pulmonary hypertension
- Post-op $PVR > 500 \text{ dsc}^{-5}$ had 30.6% mortality
- Post-op $PVR < 500 \text{ dsc}^{-5}$ had 0.9% mortality

Residual PH after PEA

Galie N and Kim NH. PATS 2006
Rationale for Medical Therapy

- Pathologic evidence of concomitant small vessel disease (Moser & Bloor ’93, Yi et al ‘00)
- Hemodynamic progression in the absence of new perfusion defects (Moser & Bloor ’93)
- Discordance between hemodynamics and radiographically apparent burden of disease (Azarian R, et al. ’97)
- Numerous uncontrolled reports of PAH-specific therapies having beneficial results in select CTEPH patients
- Availability of PAH therapy versus PEA center
“Inoperable” CTEPH: RCTs

- **Iloprost (AIR), n=57***
  6MW+FC

- **Sildenafil (UK Pilot Study), n=19**
  6MW

- **Bosentan (BENEFIT), n=157**
  6MW or PVR
CTEPH Summary

• Defining role of medical treatment 
  *(to be continued...)*

• Screen PH with VQ scan

• Refer to PEA centers
  *(not just for surgery but also for adjudication)*

• Always consider surgery
  *(operability is dependent on numerous factors)*