Surgical and Percutaneous Treatment of Chronic Thromboembolic Pulmonary Hypertension

Ehtisham Mahmud, MD, FACC
Professor and Division Chief, Cardiovascular Medicine
Director, Sulpizio Cardiovascular Center
University of California, San Diego
Disclosures

• Clinical trial/research support: Boston Scientific, Abbott Vascular, Accumetrics, Gilead Pharmaceuticals, Bristol Myers Squib, Sanofi Aventis, Corindus

• Consulting: Gilead Pharmaceuticals, St Jude, Medicines Company, Corindus, Abbott Vascular

• Speakers Bureau: Medtronic, Abbott Vascular
CTEPH – Key Points

• Unclear incidence/prevalence
• Underdiagnosed/misdiagnosed
• Delay in referral
• Obstructive disease with poor prognosis
• Medical therapy
  – Role?
  – Approved for inoperable and residual PH
    -- only one approved drug
    -- ? effect on the clot & vessels
    -- long-term efficacy
CTEPH – Key Points

• Surgery with complete Pulmonary ThromboEndarterectomy (PTE) best

• But:
  – Surgery is technically challenging, and excellent outcomes requires access to an expert center
  – Operability determination challenges
  – Access to an expert center may be limited in certain areas of the world

• Need for other forms of mechanical treatment
  – Balloon Pulmonary Angioplasty
CTEPH after Acute Pulmonary Embolism

- Becattini P et al. Chest 2006;130:172-175 ➔ 0.8% of 259 patients
- Miniati M et al. Medicine 2006;85:253-262 ➔ 1.3% of 320 patients
- Dentali F et al. Thromb Res 2009; 124:256 ➔ 8.8% of 91 patients
- Klok F et al. Haematologica 2010; 95:970 ➔ 0.57-1.5% of 866 patients

Variability in patient selection, monitoring, confirmation of diagnosis

- Guerin et al. Thromb Haemost. 2014 Sep 2;112(3):598-605
  - 146 patients, median follow up 26 months echo, CT at time of PE dx, CTEPH 4.8%

Older, prior TE events, more proximal PEs
At time of “acute PE” dx, higher PA pressures, 2 or more signs of CTED on CT
Natural History


UC San Diego
SULPIZIO CARDIOVASCULAR CENTER
CTE Disease and CTEPH:
“Got to think of the diagnosis to make the diagnosis”

• High index of suspicion in patients who have unexplained exertional dyspnea
• Absence of a known history of venous thromboembolism does not exclude CTEPH dx
• Common Diagnostic errors: COPD, asthma, deconditioning….diagnostic delays
• Diagnosis of PH should be considered in all patients with unexplained dyspnea…and CTEPH in all patients with PH
Ventilation Perfusion scan for CTE Disease

Patients with unexplained pulmonary hypertension or pulmonary hypertension and a history of pulmonary embolism

Perfusion-Scintigraphy

- Normal perfusion scan
- Indeterminate or multiple perfusion defects

CTEPH ruled out

Further imaging including CT, MR angiography, and pulmonary angiography showing evidence of CTEPH

Multidisciplinary team discussion including a specialized surgeon

Hoeper et al. Am Coll Cardiol 2009; 54:S85-S96
CTEPH: Pulmonary Angiography

◆ The ‘gold standard’
◆ Essential (in most cases) to establish operability especially for those patients with more distal disease

- Safe -- if due precautions taken
- Single injections, right and left PA
- Modification of non-ionic contrast volume / rate
- Careful patient monitoring, O2, etc.

➔ Biplane study

- “Pouch” defects
- Webs and bands
- Intimal irregularity
- Abrupt vascular narrowing
- Complete obstruction at main, lobar or segmental levels

Auger et al. Radiology 1992;182:393-8
Pulmonary Angiogram: Mapping

PA

LAT

UC San Diego
Sulpizio Cardiovascular Center
Pulmonary Endarterectomy

Successful Surgical Intervention in Severe Chronic Thromboembolic Pulmonary Hypertension

Kenneth M. Moser and Nina S. Braunwald

*Chest* 1973;64:29-35
DOI 10.1378/chest.64.1.29

UC San Diego
Sulpizio Cardiovascular Center
Surgical Principles

• Already well established\(^1,2\)
  – Median sternotomy
  – Cardiopulmonary bypass
  – Circulatory arrest
  – Bilateral endarterectomy
  – Identification of the plane
  – Complete endarterectomy

Pre vs Post PTE Surgery
PTE Results at UC San Diego

- Over 3300 cases at UCSD Medical Center
  - Mean age 53 (7 to 88)
  - Slight female predominance (50.3)
  - One third had at least one additional cardiac procedure (ASD/PFO, CABG, Valve, etc.)
  - Average operative time is about 7 hours
  - Mean CPB time $218 \pm 41$ min
  - Mean Cross clamp time $88 \pm 25$ min
  - Mean Circulatory arrest time $37 \pm 12$ min
PTE: Pre & Post-op Hemodynamics

- **PVR (dynes/sec/cm-5)**
  - Pre-op: 897 dynes/sec/cm-5
  - Post-op: 245 dynes/sec/cm-5

- **Mean PA (mm Hg)**
  - Pre-op: 45.9 mm Hg
  - Post-op: 26 mm Hg

- **Sys PA (mm Hg)**
  - Pre-op: 79 mm Hg
  - Post-op: 45 mm Hg

- **C.O. (Lit/min)**
  - Pre-op: 3.6 Lit/min
  - Post-op: 5.8 Lit/min

**UC San Diego**
**Sulpizio Cardiovascular Center**
PTE: All Cause Mortality By Era

Mortality

- Before 1990: 17%
- 1990-1998: 8%
- 1998-2006: 4.1%
- 2006-2010: 2.2%
- 2010-2014: 1%

UC San Diego
Sulpizio Cardiovascular Center
CTEPH Diagnosis
Continue lifelong anticoagulation

Operability assessment by CTEPH team

Operable
- Pulmonary endarterectomy
  - Persistent symptomatic pulmonary hypertension

Non-operable
- Recommend 2nd opinion by experienced center
- Targeted medical therapy
  - Referral for lung transplantation
  - BPA?

5th WSPH: CTEPH Treatment Algorithm
Kim NH, et al. JACC 2013
Who is not a surgical candidate?

- Operability
  - Hot topic, but in reality difficult to determine
- Surgical experience
- Center’s experience
- Patient factors:
  - Age, comorbidities, technical difficulties
- Hemodynamic vs anatomical obstruction
- Proximal versus distal disease
- Segmental versus subsegmental disease
UCSD Classification

Level I

Level II

Level III

Level IV
Level IV
Use of catheter angioscope to directly visualize internal lumen and intima of main, segmental, and subsegmental pulmonary arteries:

Olympus Angioscope

Trans-Illuminated Balloon at Tip

Normal Pulmonary Artery
Angioscopy in Chronic Pulmonary Thromboembolic Disease
Baseline V/Q scan: 74 year old woman with CTEPH
Balloon Pulmonary Angioplasty

- First described in 2001 by Feinstein et. al.
- Initial high complication rates due to pulmonary hemorrhage and death
- Advances over the last decade has made the procedure safer to be considered in certain group of patients
- Primarily Japanese experience (Okayama, Osaka and Tokyo) with few centers in Europe and USA
Baseline Right Upper Lobe Angiogram
BPA of multiple right upper lobe segments
Right Upper Lobe: Pre and Post BPA
Baseline Right Lower Lobe Angiogram
Final V/Q scan: 74 year old woman with CTEPH
Pre vs Post BPA V/Q Scan
Response to BPA: Pulmonary Pressure and PVR

Pre vs Post BPA

- Mean PAP
  - Baseline
  - Final

- PVR
  - Baseline
  - Final
Balloon Pulmonary Angioplasty

## Balloon Pulmonary Angioplasty - Results

<table>
<thead>
<tr>
<th>Number of procedures</th>
<th>Mean (SD) PVR (dyn s/cm²)</th>
<th>Peri-procedural mortality</th>
<th>Long-term survival</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before intervention</td>
<td>After intervention</td>
<td></td>
</tr>
<tr>
<td>Kataoka et al&lt;sup&gt;80&lt;/sup&gt;</td>
<td>29</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Mizoguchi et al&lt;sup&gt;81&lt;/sup&gt;</td>
<td>68</td>
<td>942 (367)</td>
<td>327 (151)</td>
</tr>
<tr>
<td>Sugimura et al&lt;sup&gt;82&lt;/sup&gt;</td>
<td>12</td>
<td>627 (236)</td>
<td>310 (73)</td>
</tr>
<tr>
<td>Fukui et al&lt;sup&gt;83&lt;/sup&gt;</td>
<td>20</td>
<td>889 (365)</td>
<td>490 (221)</td>
</tr>
<tr>
<td>Andreassen et al&lt;sup&gt;84&lt;/sup&gt;</td>
<td>20</td>
<td>704 (320)</td>
<td>472 (288)</td>
</tr>
</tbody>
</table>

PVR = pulmonary vascular resistance. NA = not available.

*Table 2: Results of balloon pulmonary angioplasty in expert centres*

Estancia La Jolla Hotel  La Jolla, California
February 26-27, 2016

Topic Highlights Include:
- Diagnostic Imaging in CTEPH
- Advances in PTE Surgery
- CTEPH and Balloon Pulmonary Angioplasty
- Role of PH Targeted Medical Therapy

Program Director: William R Auger, MD

CALL FOR ABSTRACTS & Case Reports
Deadline: NOVEMBER 15TH
Conclusions

• PTE surgery is the “gold standard” for CTEPH

• BPA is a feasible option for
  -- inoperable patients
  -- subsegmental disease
  -- post PTE residual disease

• BPA requires technical refinements

• Future investigation into optimal patient selection, appropriate endpoints and long term success required