Balloon Angioplasty For Chronic Thromboembolic Pulmonary Hypertension: Does This Really Work

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What is Chronic Thromboembolic Disease?

- Acute Pulmonary Embolus
- Incomplete resolution (>3 months AC)
- Loss of pulmonary vascular bed
- Progressive pulmonary hypertension (mean PA >25)
- Right heart failure

CTE Disease and CTEPH: “Have 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
- THE MOST CURABLE FORM OF PULMONARY HYPERTENSION
Natural History

Pulmonary ThromboEndarterectomy
- Well established therapy:
  - Median sternotomy
  - Cardiopulmonary bypass
  - Circulatory arrest
  - Bilateral endarterectomy
  - Identification of the plane
  - Complete endarterectomy

UCSD Classification


PTE: Pre & Post-op Hemodynamics

Survival, 3-year, operated vs not operated

Quality of life dramatically improved post-op!

Surgical risk assessment pre-PTE
- Age, functional status/frailty assessment.
- Presence of other comorbidities, suitability for median sternotomy, LV function, coagulopathy/bleeding risk
- Surgeon Experience
- Proximal versus distal disease (Segmental versus subsegmental)
**CTEPH – Key Points**

- Surgery with complete Pulmonary ThromboEndarterectomy (PTE) – likely best
- But:
  - Surgery technically challenging...excellent outcomes requires access to an expert center
  - Determination of "Operability" can be challenging
- Need for other forms of mechanical treatment
  - Balloon Pulmonary Angioplasty

**Balloon Pulmonary Angioplasty**

- 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 UC San Diego

**BPA for CTEPH**

- Aim to disturb the luminal obstruction which is web-like fibrinous organized clot, and restore blood flow.

**OFDI and IVUS Imaging of CTEPH**

- OCT image from the Satoh group
  - Tokyo 06/2015
- Aim: rupture endovascular membranes and dilate stenoses
Patient presentation

• 42 year old male with PMHx of PE (2011) while residing in India
  – Initially tx with Warfarin for 4 years → switched to Xarelto → stopped taking in 5/2017
  – Admitted with dyspnea in 9/2017 and was found to have severe pHTN on TTE
  – Evidence of CTEPH on V/Q scan

VQ Scan (12/2017)

Baseline Right Lung (AP / Lateral) – 12/2017

Baseline Left Lung (AP / Lateral) – 12/2017

Patient presentation (cont.)

• Hemodynamics
  – RA 9, PA 123/33 (69), PCWP 16, PVR 10.1 WU
  – CO 5.3 L/min, CI 2.9 L/min/m2

• Deemed appropriate surgical candidate for PTE
• Refused surgery
• Started on Riociguat 0.5 mg TID
• Decision to proceed with balloon pulmonary angioplasty

BPA #1 – 1/2018 (1st Right Lung session)
A) Baseline B) s/p BPA #1

BPA #3 – 3/2018 (2nd Right Lung session)

A) Baseline B) s/p 2nd RL BPA

Baseline Resting Pressure Gradient

Pressure Gradient After First Balloon Angioplasty

Pressure Gradient After Final Balloon Angioplasty
BPA #5 – 5/2018 (3rd Right Lung session)

Baseline Left Lung (AP / Lateral) – 12/2017

BPA #2 – 2/2018 (1st Left Lung session)

A) Baseline B) s/p BPA #2 (1st Left Lung session)

BPA #4 – 3/2018 (2nd Left Lung session)

BPA #6 – 6/2018 (3rd Left Lung session)
A) Baseline B) s/p BPA #6

BPA #7 – 7/2018 (4th Right Lung session)

V/Q scans

Hemodynamics

EKG (12/6/17) – pre - BPA

EKG (6/25/18) – resolution of right axis deviation

- Marked improvement in function capacity
- Resolution of chest pressure
- Riociguat uptitrated earlier in the year from 0.5 to 2.5 TID, however, Macitentan was never added given significant improvement of his hemodynamics
MGH experience (as of 5/18)

- Total 11 patients and 39 BPA sessions
- Average of 4 sessions of BPA performed for each patient.
- No mortality

PA (mean)

PVR (dynes)

CI (L/min/m²)

Outcomes of Balloon Pulmonary Angioplasty in Europe

<table>
<thead>
<tr>
<th>Year</th>
<th>First author, Country</th>
<th>Patient number</th>
<th>Procedures</th>
<th>Complications (%)</th>
<th>In-hospital death rate (%)</th>
<th>Follow-up Period (months)</th>
<th>Mean PAP (mmHg)</th>
<th>Baseline Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>2001</td>
<td>Feinstein [1] USA</td>
<td>18</td>
<td>48</td>
<td>61.0</td>
<td>5.6</td>
<td>33</td>
<td>21.9±12.1</td>
<td>-9.0</td>
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<tr>
<td>2013</td>
<td>Andreasen [2] Norway</td>
<td>20</td>
<td>73</td>
<td>35.0</td>
<td>10.0</td>
<td>51</td>
<td>13.0±11.0</td>
<td>-12.0</td>
</tr>
<tr>
<td>2015</td>
<td>KURZYNA [3] Poland</td>
<td>20</td>
<td>37</td>
<td>10.0</td>
<td></td>
<td>45</td>
<td>18.0±6.0</td>
<td>-17.0</td>
</tr>
<tr>
<td>2016</td>
<td>Roik [4] Poland</td>
<td>9</td>
<td>27</td>
<td>5.5</td>
<td></td>
<td>5</td>
<td>10.0±8.0</td>
<td>-5.4</td>
</tr>
<tr>
<td>2017</td>
<td>Olsson [5] Germany</td>
<td>56</td>
<td>266</td>
<td>9.4</td>
<td></td>
<td>24</td>
<td>1.8±2.0</td>
<td>40.0±12.0</td>
</tr>
<tr>
<td>2018</td>
<td>Wiedenroth [7] Germany</td>
<td>10</td>
<td>35</td>
<td>2.9</td>
<td>0</td>
<td>6</td>
<td>21.0±2.0</td>
<td>-0</td>
</tr>
<tr>
<td>2018</td>
<td>Lang Austria</td>
<td>97</td>
<td>468</td>
<td>4.3</td>
<td>2</td>
<td>36</td>
<td>45.4±11.1</td>
<td>-19.0</td>
</tr>
</tbody>
</table>

a: Reperfuison pulmonary edema, b: Severe lung injury

Hemodynamics

*For subjects with mPAP >30 and ≥3 BPA procedures
**UC San Diego BPA Registry**

### WHO Functional Class

- Pre-BPA: [Chart showing functional class distribution]
- Post-BPA: [Chart showing functional class distribution]

*For subjects with mPAP >30 and ≥3 BPA procedures*

**UC San Diego BPA Registry**

### 6-Minute Walk Distance

- Pre-BPA: 361 m
- Post-BPA: 420 m

*For subjects with mPAP >30 and ≥3 BPA procedures*

**UC San Diego BPA Registry - COnplications**

<table>
<thead>
<tr>
<th>Complication</th>
<th>Count</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoptysis</td>
<td>13</td>
<td>7.7%</td>
</tr>
<tr>
<td>Lung vascular injury</td>
<td>3</td>
<td>1.8%</td>
</tr>
<tr>
<td>Reperfusion lung edema</td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td>Non-invasive PPV</td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td>Intubation</td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td>Acute kidney injury</td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td>Inpatient death</td>
<td>0</td>
<td>0%</td>
</tr>
</tbody>
</table>

*For subjects with mPAP >30 and ≥3 BPA procedures*

**Tools for Balloon Pulmonary Angioplasty**

- **Yes**
  - Pressure wire/catheter
  - Sculpting/scoring balloons

- **No**
  - Polymer jacketed wires
  - Cutting balloon

**Image Guided Treatment: IVUS or OCT ?**

Lang et al. Eur Respir J 2017; 50: 160119

**Check List for Team BPA**

- Interventional cardiologist, pulmonary vascular medicine, CT surgery
- Credentialing
- Training and Proctoring
- Equipment
- 24 hours telemetry/IMU
- Outcomes and Quality Assurance
- ICU for any intra-procedural adverse events
- Limit procedure contrast to 400cc and radiation to 2 Gyr
Conclusions- Yes, BPA does work!

- Multidisciplinary planning meeting prior to case
- Determine necessary patient preparation.
  - Anticoagulation Management
  - Testing
  - Interval of Procedures
- Procedure planning
  - Imaging
  - Guidance
  - Technique and equipment

CTEPH occurs in up to 1-3% of patients with an acute pulmonary embolism
- PTE surgery is the current definitive therapy for CTEPH
- BPA is a feasible therapeutic option for CTEPH patients with:
  - inoperable disease
  - segmental/subsegmental disease
  - post PTE residual disease
- Requires significant technical refinement and development of dedicated equipment
- BPA should be physiology based: perfusion scans and invasive hemodynamic measurements
- Requires dedicated program and skilled/careful operator...no cowboys/girls allowed!
- Future investigation for BPA to focus on:
  - optimal patient selection/acquisition of objective adjudicated data
  - standardized technique and procedural endpoints
  - long-term patency and clinical success
  - randomized controlled trials

Conclusions

- Careful evaluation at a CTEPH center is excellence is gold standard.
- Pulmonary thrombo-endarterectomy remains first line therapy.
- All patients should be evaluated by an experienced surgeon for operability assessment.
- BPA is currently reserved for those who are either non-operable or not expected to benefit from surgery.
- BPA is a promising therapy and we need more evidence to better help with patient selection in such cases.

PERT: Future of PE Management

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...attend the annual PERT Business and PE CME Meetings in BOSTON! October 2019