Balloon Pulmonary Angioplasty for CTEPH: Overview of an emerging therapy

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Assistant Professor of Medicine/ Interventional Cardiology
Disclosure Statement of Financial Interest

I, Vikas Aggarwal DO NOT have a financial interest/arrangement or affiliation with one or more organizations that could be perceived as a real or apparent conflict of interest in the context of the subject of this presentation.
Angiographic Appearance CTEPH
PTE Surgery is currently standard of care.
Only half of all patients with CTEPH get PTE Surgery
What is Balloon Pulmonary Angioplasty
History

**First case report 1988**

Recently we treated a patient with multiple pulmonary artery stenoses and pulmonary hypertension caused by pulmonary embolism by means of balloon angioplasty. This promising therapeutic alternative has not been described before.

**First Case Series 2001**

**Balloon Pulmonary Angioplasty for Treatment of Chronic Thromboembolic Pulmonary Hypertension**

Jeffrey A. Feinstein, MD, MPH; Samuel Z. Goldhaber, MD; James E. Lock, MD; Susan M. Ferndandes, PA-C; Michael J. Landzberg, MD

- **18 Patients**
- mPAP 43.0+/-12.1 to 33.7+/-10.2 mmHg (P 0.007)
- vessels remained patent on follow-up
- (61%) → Reperfusion Pulmonary Edema
- (17%) → Mechanical Ventilation
- (5.6%) → Mortality

CHEST 1988 94:1249-53

CHEST 1988 94:1249-53
Initial Japanese Experience

- 68 patients – 255 sessions
- 4 (2-8) sessions per patient
- Vascular injury 60%
- 6% required mechanical ventilation
- 1 death (1.5% mortality)

Table 1. Clinical and Hemodynamic Data Before and After BPA

<table>
<thead>
<tr>
<th>WHO functional class (I/II/III/IV)</th>
<th>Before BPA (n=68)</th>
<th>After BPA (n=67)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxygen inhalation (L/min)</td>
<td>3.0±1.4</td>
<td>1.3±1.0</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>6MWD, m</td>
<td>296±108</td>
<td>366±83</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>BNP, pg/mL</td>
<td>330±444</td>
<td>35±55</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>sPAP, mm Hg</td>
<td>81.3±16.9</td>
<td>42.3±11.9</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>dPAP, mm Hg</td>
<td>24.3±7.1</td>
<td>13.4±4.8</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>mPAP, mm Hg</td>
<td>45.4±9.6</td>
<td>24.0±6.4</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>RAP, mm Hg</td>
<td>8.1±4.4</td>
<td>1.9±1.5</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>CI, L/min/m²</td>
<td>2.2±0.7</td>
<td>3.2±0.6</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>PVR, dyno sec/cm²</td>
<td>942±367</td>
<td>327±151</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

Values other than WHO functional class are expressed as mean±SD. WHO functional class is presented as the median and number of patients in each class.

6MWD indicates 6-minute walking distance; BPA, balloon pulmonary angioplasty; BNP, brain natriuretic peptide; CI, cardiac index; dPAP, diastolic pulmonary arterial pressure; mPAP, mean pulmonary arterial pressure; PVR, pulmonary vascular resistance; RAP, right atrial pressure; sPAP, systolic pulmonary arterial pressure; and WHO, world health organization.
Representative BPA Procedure

Pre and Post BPA Right Lower Lobe (A8, 9, 10): Pressure Gradient Based

A8: BPA with 2.0 and 3.0 balloon
A9: Pd/Pa based with improvement from 0.40 to 0.52 to 0.82 with 2.0 to 3.0 to 4.0 balloons
A10: BPA with 2.0 and 3.0 balloons
Representative BPA Procedure

Pre and Post BPA Right Lower Lobe (A8, 9, 10): Pressure Gradient Based
BPA setup: Like Any other PCI Procedure
BPA Equipment and Approach in USA (2018)

- Single plane angiography (biplane for diagnostic)
- 8-9F venous access sheath: femoral rather than internal jugular
- 6-7F long sheath telescoped through 9F introducing sheath
- 6F guide catheter: multipurpose, Judkins right, Hockeystick, EBU
- Anticoagulation: heparin with ACT 200-250s
- Contrast: 50/50
- 0.014” guide wires; no polymer jacketed wires
- 2-5 mm compliant; NC or Sculpting balloon catheters for recalcitrant
- IVUS and OCT rarely used
- Increasingly using resting pressure gradients (Pd/Pa) to target and optimize

Mahmud et al. Interv Cardiol Clin 2018;7:103-117
BPA Treatment Approach

• Anticipate 2-6 sessions necessary per patient
• 2 sessions over 3-7 days with one lung each time
• Return 1-3 months for subsequent sessions
• Conscious sedation
• Parameters being followed
  • V/Q
  • ECHO
  • NT pro BNP
  • 6 MW
  • Hemodynamics
• Admitted for monitoring – usually 24 hours
• Started on heparin infusion post-procedure

Mahmud et al. Interv Cardiol Clin 2018;7:103-117
Tools for Balloon Pulmonary Angioplasty

- Yes
  - Pressure wire or catheter
  - Scoring or sculpting balloon

- No
  - Polymer jacketed wires
  - Cutting balloon

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Challenges of BPA
Technical Challenges of BPA

- To engage the target branch
  - Especially, to select the branches in middle lobe or lingular segment

- To find the target lesion
  - Especially, to find intravascular web lesion

- To cross the target lesion
  - Most lesions exist at bifurcation or orifice of branches

- Distal vessels in some lesions are invisible by PAG
  - To select the appropriate balloon size

- To dilate the lesion
  - Guiding catheter is always swinging along with heartbeat and breathing
Pressure catheter guided BPA
Dual Energy CT perfusion imaging
Pressure-Wire-Guided Percutaneous Transluminal Pulmonary Angioplasty
A Breakthrough in Catheter-Interventional Therapy for Chronic Thromboembolic Pulmonary Hypertension

Takumi Inami, MD,* Masaharu Kataoka, MD,† Nobuhiro Shimura, MD,† Haruhisa Ishiguro, MD,* Ryoji Yanagisawa, MD,* Keiichi Fukuda, MD,† Hideaki Yoshino, MD,* Toru Satoh, MD*
Long-term Outcomes after BPA for CTEPH

Representative staged procedure of current BPA

Initial dilation

before

after

Second dilation (1 month later)
Evaluation at a Center of Excellence

MULTIDISCIPLINARY TEAM

- Pulmonary HTN specialist.
- Experienced Cardiothoracic Surgeon.
- BPA Interventionalist.
- Diagnostic chest radiologist
- Vascular medicine expertise.
- Acceptable surgical outcomes (<5% in hospital mortality).

All patients with CTEPH should be evaluated at a center of excellence.

Anticoagulation

Operability Assessment

Clinical Syndrome, Comorbidities and Surgical Risk Assessment

Anatomic and Hemodynamic Considerations

Standard of Care in 2018
KEY QUESTIONS

- Does the burden of obstructive disease correlate with observed hemodynamic impairment and symptoms?
- Are the diseased vessels surgically accessible?
- Do patient comorbidities make PTE less attractive option?
Anatomic Considerations

Severely Elevated Pulmonary Vascular Resistance in CTEPH

Disease Location And Burden

Obstructive Component
- Proximal
- Distal
- Both

Distal non obstructive Pulmonary Arteriopathy
- Defined as subsegmental disease
Extensive bilateral disease best treated with surgery
Lesion Suitability for BPA

Ring like stenosis

Lesion Suitability

Ring like stenosis
Web like stenosis

Lesion Suitability

Ring like stenosis

Web like stenosis

Sub total occlusion

Lesion Suitability

- Ring like stenosis
- Web like stenosis
- Sub total occlusion
- Total occlusion

Lesion Suitability

- Ring like stenosis
- Web like stenosis
- Sub total occlusion
- Total occlusion
- Severe Tortuosity


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Lesion Suitability

Ring like stenosis

Web like stenosis

Sub total occlusion

Total occlusion

Severe Tortuosity

BPA Most Successful

BPA least successful

Lesion Suitability

Ring-like stenosis

<table>
<thead>
<tr>
<th>Description of Lesion Type</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>E</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number, n</td>
<td>248</td>
<td>1235</td>
<td>342</td>
<td>67</td>
<td>44</td>
</tr>
<tr>
<td>Bifurcation lesion, n (%)</td>
<td>248 (100)</td>
<td>1092 (88.4)</td>
<td>301 (88.0)</td>
<td>61 (91.0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Success, n (%)</td>
<td>248 (100)</td>
<td>1219 (98.7)</td>
<td>296¢(86.5)</td>
<td>35 (52.2)</td>
<td>28 (63.6)</td>
</tr>
<tr>
<td>Complication, n (%)</td>
<td>4 (1.6)</td>
<td>27 (2.2)</td>
<td>53¢ (15.5)</td>
<td>4 (6.0)</td>
<td>19 (43.2)</td>
</tr>
</tbody>
</table>

Type of complication

<table>
<thead>
<tr>
<th></th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>E</th>
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</thead>
<tbody>
<tr>
<td>Balloon injury, n</td>
<td>3</td>
<td>7</td>
<td>5</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Wire injury/perforation, n</td>
<td>0</td>
<td>12</td>
<td>41</td>
<td>4</td>
<td>19</td>
</tr>
<tr>
<td>Dissection of vessels, n</td>
<td>1</td>
<td>8</td>
<td>7</td>
<td>0</td>
<td>0</td>
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BPA least successful

**Lesion Suitability**

### Description of Lesion Type

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<td>0 (0)</td>
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<tr>
<td>Subtotal Stenosis</td>
<td>296$ (86.5)</td>
<td>351 (52.2)</td>
<td>28 (63.6)</td>
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<tr>
<td>Subtotal Occlusion</td>
<td>53$ (15.5)</td>
<td>4 (6.0)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Total Occlusion</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tortuous</td>
<td></td>
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### Success, n (%)

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<td>0</td>
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<td>41</td>
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<td>1</td>
<td>8</td>
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<td>0</td>
</tr>
</tbody>
</table>


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**BPA Most Successful**

**BPA least successful**

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**Total occlusion**

**Severe Tortuosity**

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Thoracic BPA complications

• **Lung injury** (clinically: hypoxemia, hemoptysis, lung opacities, lung edema)

  ➢ Vascular Injury (-guiding catheter, -balloon, -wire)
    ➢ Perforation
    ➢ Dissection
    ➢ Thrombosis

  ➢ Bleeding
  ➢ Pulmonary Infection
  ➢ Reperfusion?
Non-Thoracic BPA complications

• Arrhythmia
• Renal dysfunction-failure
• Allergic reactions
• Radiation injury
• Access site complications
## Reperfusion Pulmonary Edema

<table>
<thead>
<tr>
<th>Grade</th>
<th>Definition of Graded RPE</th>
<th>Number of Procedures</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>No significant recognition of reperfusion pulmonary edema on chest x-ray</td>
<td>87 (62)</td>
</tr>
<tr>
<td>2</td>
<td>Mild or small reperfusion pulmonary edema on chest x-ray, but automatic improvement with only a small increase in oxygen for a few days</td>
<td>35 (25)</td>
</tr>
<tr>
<td>3</td>
<td>Moderate reperfusion pulmonary edema on chest x-ray that needed elevated concentration of oxygen administered via oxygen mask to maintain arterial saturation at optimum level</td>
<td>9 (6)</td>
</tr>
<tr>
<td>4</td>
<td>Moderate to severe reperfusion pulmonary edema on chest x-ray needing non-invasive positive pressure ventilation with high-concentration oxygen inhalation</td>
<td>7 (5)</td>
</tr>
<tr>
<td>5</td>
<td>Extremely severe reperfusion pulmonary edema on chest x-ray needing artificial ventilation</td>
<td>2 (1)</td>
</tr>
</tbody>
</table>

Values are n (%). 
RPE = reperfusion pulmonary edema.

Management of Acute Hemoptysis During BPA

1. Immediate balloon tamponade of the injured vessel
2. Oxygenation management including oropharyngeal suctioning, supplemental oxygen, non-invasive positive pressure ventilation (mechanical ventilation/ECMO)
3. Cessation/reversal of anticoagulation
4. Repeat prolonged balloon tamponade as necessary
5. For persistent pulmonary hemorrhage consider bailout transcatheter coil embolization, covered stent implantation, and/or gel foam/adipose injection

Mahmud et al. Interv Cardiol Clin 2018;7:103-117
Outcomes of BPA

308 patients treated in Japanese 7 centers between 2004 – 2013

<table>
<thead>
<tr>
<th></th>
<th>Before BPA (n=308)</th>
<th>After BPA (n=249)</th>
<th>At Follow-Up (n=196)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>WHO FC (median)</td>
<td>3</td>
<td>2*</td>
<td>2*</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>6MWD, m</td>
<td>318.1±122.1</td>
<td>401.3±104.8*</td>
<td>429.7±108.5*</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BNP, pg/mL</td>
<td>239.5±334.2</td>
<td>43.3±76.4*</td>
<td>38.7±71.2*</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HR, bpm</td>
<td>74.9±13.6</td>
<td>70.8±11.9*</td>
<td>67.3±11.0*</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>mPAP, mm Hg</td>
<td>43.2±11.0</td>
<td>24.3±6.4*</td>
<td>22.5±5.4*</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>RAP, mm Hg</td>
<td>6.5±4.1</td>
<td>3.2±2.4*</td>
<td>4.7±3.0*</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PAWP, mm Hg</td>
<td>8.6±3.3</td>
<td>7.3±3.1*</td>
<td>8.3±3.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CI, L-min⁻¹·m⁻²</td>
<td>2.6±0.8</td>
<td>2.9±0.7*</td>
<td>2.8±0.6†</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SvO₂, %</td>
<td>66.3±9.1</td>
<td>71.5±8.0*</td>
<td>68.8±6.4*</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PVR, dyne·sec·cm⁻⁵</td>
<td>853.7±450.7</td>
<td>359.5±222.6*</td>
<td>288.1±194.5*</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SaO₂, %</td>
<td>93.3±4.5</td>
<td>96.1±4.4*</td>
<td>94.0±5.2</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Values are expressed as mean±SD unless otherwise specified. P value in the right column indicates the P value among 3 data points. 6MWD indicates 6-minute walk distance; BNP, B-type natriuretic peptide; BPA, balloon pulmonary angioplasty; CI, cardiac index; HR, heart rate; mPAP, mean pulmonary artery pressure; PAWP, pulmonary arterial wedge pressure; PVR, pulmonary vascular resistance; RAP, right atrial pressure; SaO₂, arterial oxygen saturation; SvO₂, mixed venous oxygen saturation; and WHO FC, World Health Organization functional class.

*P<0.001 and †P<0.01 versus before BPA in post hoc analysis.

Mid term survival after BPA

308 patients treated in Japanese 7 centers between 2004 – 2013

Complications occurred in 511 procedures (36.3%)
### Outcomes of BPA at Okayama medical center


<table>
<thead>
<tr>
<th>Metric</th>
<th>Before BPA (n = 384)</th>
<th>After BPA (n = 334)</th>
<th>Follow-up (n = 260)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>6MWD (m)</strong></td>
<td>275 ± 138</td>
<td>382 ± 106*</td>
<td>406 ± 134*</td>
</tr>
<tr>
<td><strong>Systolic PAP (mmHg)</strong></td>
<td>71.9 ± 21.2</td>
<td>38.9 ± 9.2*</td>
<td>34.6 ± 9.1*</td>
</tr>
<tr>
<td><strong>Mean PAP (mmHg)</strong></td>
<td>41.5 ± 11.9</td>
<td>23.5 ± 5.3*</td>
<td>21.1 ± 5.3*</td>
</tr>
<tr>
<td><strong>RAP (mmHg)</strong></td>
<td>7.0 ± 4.2</td>
<td>4.3 ± 3.2*</td>
<td>4.7 ± 2.9*</td>
</tr>
<tr>
<td><strong>CI (L/min/m²)</strong></td>
<td>2.7 ± 0.8</td>
<td>2.9 ± 0.8*</td>
<td>2.6 ± 0.6</td>
</tr>
</tbody>
</table>

BPA, balloon pulmonary angioplasty; follow-up, 2.5 ± 1.8 years (range, 0.3 – 8.8 years) after the final BPA; 6MWD, 6-minute walking distance; PAP, pulmonary artery pressure; RAP, right atrial pressure; CI, cardiac index; PVR, pulmonary vascular resistance; *, p < 0.05 vs. before BPA.

The patient numbers before BPA include 10 cases of in-hospital death (in-hospital mortality rate, 2.6%).
Outcomes of BPA at Okayama medical center
(Nov 2004 – Jun 2018, n=384)

<table>
<thead>
<tr>
<th></th>
<th>Initial half (n = 192)</th>
<th>Later half (n = 192)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>60.2 ± 12.5</td>
<td>62.9 ± 13.1</td>
<td>0.046</td>
</tr>
<tr>
<td>Women</td>
<td>152 (79.2%)</td>
<td>148 (77.1%)</td>
<td></td>
</tr>
<tr>
<td>WHO FC (I/II/III/IV)</td>
<td>2/25/128/37</td>
<td>0/62/103/27</td>
<td></td>
</tr>
<tr>
<td>mPAP (mmHg)</td>
<td>42.7 ± 11.9</td>
<td>40.4 ± 11.8</td>
<td>0.051</td>
</tr>
<tr>
<td>CI (L/min/m²)</td>
<td>2.7 ± 0.8</td>
<td>2.7 ± 0.7</td>
<td>0.978</td>
</tr>
</tbody>
</table>

Values are expressed as mean ± SD except for WHO FC.
BPA, balloon pulmonary angioplasty; WHO FC, world health organization functional class; mPAP, mean pulmonary artery pressure; CI, cardiac index; PVR, pulmonary vascular resistance.
Long term survival after BPA at Okayama medical center


- In hospital death: 10 cases
- Deaths during follow up: 3 cases
- Right hear failure: 3 cases
Long term survival after BPA at Okayama medical center


Cumulative survival rate
Time after initial BPA (year)

Initial half patients (n = 192)

Later half patients (n = 192)

P=0.042

Patients at risk

<table>
<thead>
<tr>
<th>Time after initial BPA (year)</th>
<th>192</th>
<th>177</th>
<th>176</th>
<th>174</th>
<th>170</th>
<th>149</th>
<th>92</th>
<th>28</th>
<th>6</th>
<th>2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients at risk</td>
<td>192</td>
<td>152</td>
<td>113</td>
<td>75</td>
<td>34</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>
• PTE/PEA is the definitive and preferred choice for treatment of CTEPH
• In most patients, PTE/PEA can be potentially curative
• As a general rule, segmental disease can be considered as the limit of surgical accessibility, and PTE/PEA should always be considered as the first option.
• Disease accessibility can vary between surgeons and patients, and many factors contribute to the decision making, including a concordance of disease and severity of PH.
Conclusion

• Determination of the best treatment approach needs a multidisciplinary evaluation by an expert CTEPH team.

• Surgery, BPA, and/or Medical therapy should be thought of as complimentary, as opposed to independent and unrelated.

• Ultimately, patients will have the most benefit from an unbiased multidisciplinary team of experts.

• Key ingredient to success is an excellent and dedicated team.
Conclusion

BPA should be physiology based: perfusion scans and invasive hemodynamic measurements.

Future investigation for BPA to focus on:
- optimal patient selection and acquisition of objective adjudicated data.
- standardized technique and procedural endpoints.
- long-term patency and clinical success.
- role of BPA in chronic thrombo-embolic disease.
Acknowledgement

• Henry Ford Hospital Pulmonary Embolism and Pulmonary Hypertension Programs.

• Michigan Medicine Pulmonary Embolism and Pulmonary Hypertension Programs.