Understanding Pulmonary Hypertension

*pearls and pitfalls of patient assessment…
and a few cases*

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70 yo man with 8 months of progressive dyspnea.

Occasional PND. No angina, syncope.

PMH: hypertension, CKD, s/p renal transplant in 2003

Exam: Not cyanotic. Dyspnea with speaking. SpO2 98% RA, HR 90, BP 150/80, RR 20


Echo: RVSP by Doppler 78 mmHg
Can hardly breathe….RV big, but normal RV systolic function. Hmmm…. 

RHC: RA 10, PA 75/30, wedge 28 (V waves 45), CO 11 lpm, PVR 2

Diagnosis: high output heart failure ➔ close fistula ➔ symptoms resolved
Blood pressure 160/100

Diagnosis → systemic hypertension

Hemoglobin 7

PASP

Diagnosis?

Doppler

70 mmHg (or by RHC)

High CO HF-AV fistula

Severe COPD

Acute MR-HF

PAH

Overestimated PASP-no PH at all
Pulmonary Hypertension: Diagnosis or Diagnostic Category?

- PH is a diagnostic category
- PH is a heterogeneous disorder
- PH arises from interaction b/w pulmonary blood flow, pulmonary artery impedance, and pulmonary venous pressure
- Thus, PH may result from any of these factors, or a combination thereof
Pulmonary Hypertension

Clinical Classification

- Group 1: Idiopathic PAH (primary) and associated conditions (CTD, anorexigen, portopulmonary, left-right shunt, HIV, etc)
- Group 2: Pulmonary venous hypertension (due to left heart disease)
- Group 3: Pulmonary hypertension associated with chronic respiratory disorder(s) (CRDs) and/or hypoxemia
- Group 4: Pulmonary hypertension due to chronic thrombotic/embolic disease
- Group 5: Miscellaneous

Pathophysiology of PAH

**Normal**
- High flow, low resistance vessel

**PAH**
- Low flow, high resistance vessel
- Increased PVR
- RV dysfunction → failure

Adapted from Gaine S. *JAMA*. 2000;284:3160-3168.
PAH: Definition

- Sustained elevation of mean pulmonary arterial pressure:
  >25 mm Hg at rest

  _with_

  -(end-expiratory) pulmonary capillary wedge pressure (PCWP) <15 mm Hg and
  \[ PVR = \frac{mPAP - PCWP}{CO} \]
Progression of PAH
Is There a Reason to Suspect PAH?

**History**

- Dyspnea on exertion
- Fatigue
- Syncope, pre-syncope (often repeated syncope)
- Angina
- Heart failure–LE edema
- Raynaud’s

Is There a Reason to Suspect PAH?

Risk Factors

- Family history
- Connective tissue disease
- Congenital heart disease
- Portal hypertension—OLT candidate
- Environmental/drug factors
- HIV
Is There a Reason to Suspect PAH?

**Physical Exam**

### Presence of PH
- Loud P2
- Left parasternal lift
- Systolic murmur (TR)
  - Often high pitch (sounds like MR)
- RV S4

### Presence of RV Failure
- ↑ JVP (V>A)
- RV S3
- Hepatomegaly
- Edema
- Ascites
Is There a Reason to Suspect PAH?

ECG

Is There a Reason to Suspect PAH?

*Chest X-Ray*

A-P or P-A in PAH

Lateral in PAH

Lateral in normal

Prominent proximal pulmonary arteries

Loss of retrosternal air space
Is There a Reason to Suspect PAH?

**PFTs/Functional Assessment**

- Always obtain ‘full’ PFTs in PH workup (spirometry, lung volumes, DLCO)
- ‘Classic’ pattern in PAH → normal spirometry + DLCO
- 6-minute-walk test: 6MWD variable (often reduced), commonly with drop in SpO$_2$ with ambulation
CTEPH : A PAH ‘Mimic’
Don’t Forget the VQ Scan...

**MISSED DIAGNOSIS OF CTEPH....**
Is There a Reason to Suspect PAH?

Patient evaluation
- Full history and physical examination
- Chest x-ray
- Electrocardiogram

Suspicion of PAH persists

Echocardiogram

Patient typically not referred for RHC

RHC to evaluate precise hemodynamics

# Basic Principles of Echocardiography

<table>
<thead>
<tr>
<th>Technique</th>
<th>Key Features</th>
</tr>
</thead>
<tbody>
<tr>
<td>M-mode</td>
<td>Records/measures positions and movements of heart, cardiac dimensions, and motion patterns</td>
</tr>
<tr>
<td>2-D</td>
<td>Produces 2-D cross-sectional “slice” of heart, providing information about heart structure and spatial relationships during cardiac cycle</td>
</tr>
<tr>
<td>Doppler</td>
<td>Evaluates blood flow through heart; assesses direction and velocity of blood flow through heart</td>
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</tbody>
</table>


Caution: Doppler estimates pressure...

Bland Altman RVSP vs. PASP by Cath

Bias > 20 with good or excellent quality TR jet

Bias > 20 with fair or poor quality TR jet

The RV is ‘where it’s at’ in PAH...

*look at the heart...not the lungs*

Remember the 3 S’s

**SIZE**-RV dilation

**SQUEEZE**-RV function

**SMUSH**-septal flattening, LV compression from RV
Size-RV dilatation

Normal

RV:LV < 1.0

PAH (severe)

RV:LV ≥ 1.0

Squeeze

What is true for LV…not for RV

RV contracts more like a piston or a plunger…
It’s not the pressure….but RV function that dictates outcome

Unadjusted HR 5.7
Log rank $\chi^2$ 6.8
$P$-value=0.009

Forfia et al, AJRCCM Nov 2006
Smush-severe
Notching of Doppler \textsubscript{RVOT} detects ↑ PVR and ↓ RV function in PH referral cohort

Pulsed-wave Doppler in RV outflow tract

<table>
<thead>
<tr>
<th>mPAP (mm Hg)</th>
<th>33</th>
</tr>
</thead>
<tbody>
<tr>
<td>PVR (Wood unit)</td>
<td>3.3</td>
</tr>
<tr>
<td>TAPSE (cm)</td>
<td>2.2</td>
</tr>
<tr>
<td>Ecc index</td>
<td>1.1</td>
</tr>
</tbody>
</table>

Ecc, eccentricity; Ecc index, Eccentricity index; LSN, late systolic notch; MSN, mid-systolic notch; mPAP, mean pulmonary arterial pressure; PVR, pulmonary vascular resistance; RV, right ventricle; TAPSE, tricuspid annular plane systolic excursion.

The Right Heart Cath:
- the gold standard for PAH diagnosis
- required for patients with suspected PAH

PAH (Group 1)
Hypoxic/Lung CTEPH

Fever
Thyrotoxicosis
Anemia
Pregnancy
Some PoPH

Oximetry ‘run’ to assess for left→right shunt
Case 1

History: 63 y.o. woman with 2 years severe dyspnea. Dyspnea has not progressed. Reports occasional PND. Denies angina, syncope. 2+ LE edema persistent over the past 2 years. Dyspnea with mild to minimal activity.

PMH:
- systemic hypertension
- OSA
- obesity


Echo: Normal LV size, function. Mild left ventricular hypertrophy. RVSP by Doppler 40-45mmHg.
Clinical pearls in PH…

History: 63 y.o. woman with 2 years severe dyspnea. Dyspnea has not progressed. Reports occasional PND. Denies angina, syncope. 2+ LE edema persistent over the past 2 years. Dyspnea with mild to minimal activity.

PMH:
- systemic hypertension
- OSA
- obesity

Other relevant history

- Patient diagnosed with idiopathic pulmonary arterial hypertension 2.5 years ago.
- A right heart catheterization was never performed.
- Patient initially treated with sildenafil, 20 mg TID.
- 4 months later, bosentan added when patient failed to report any symptomatic improvement.
- Patient’s symptoms have not improved. In fact, symptoms may have worsened somewhat over this time period.
What is most likely explanation for why this patient’s dyspnea has not improved on PH specific therapy?

A. The patient’s PAH has progressed despite PH specific therapy.
B. The patient does not have PAH.
C. The patient’s sleep apnea has led to severe pulmonary hypertension that has been relatively resistant to PH medical therapy.
D. Most patients with PAH do not experience symptomatic improvement on medical therapy-just a delay in time to worsening.
PASP ≈ 40 mmHg

TR Vmax
Vmax 263 cm/s
Max PG 28 mmHg

PASP ≈ 40 mmHg
• LAE. LVH. Although not optimal view of RV, function appears reasonable. No paradoxial septal motion. No dilated CS.
• No evidence of septal flattening...
• RV:LV ratio < 1.0; LA larger than RA.
• RV not apex ‘sharing’ or apex forming
• Sharp angle at RV apex

- Normal RV function: TAPSE 2.3-2.7 cm
- Mild RVD: TAPSE 1.9-2.2 cm
- Mod RVD: TAPSE 1.5-1.8 cm
- Severe RVD: TAPSE < 1.5 cm
Let’s integrate the echo-Doppler findings….

‘LEFT’

Normal RV function
Normal RV size, shape (apical angle)
No septal flattening
LAE
Moderate LVH
No notch Doppler RVOT
Grade III DD

‘RIGHT’
Question:

What is the most appropriate next step in this case?

A. Increase sildenafil to 40 mg TID
B. Add inhaled Iloprost
C. Aggressive systemic BP management
D. Perform right heart catheterization

D. Perform right heart catheterization
Right heart catheterization

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RA</td>
<td>15 mmHg</td>
</tr>
<tr>
<td>PA</td>
<td>47/25 (32) mmHg</td>
</tr>
<tr>
<td>Wedge pressure</td>
<td>25 mmHg</td>
</tr>
<tr>
<td>Transpulmonary gradient</td>
<td>7 mmHg</td>
</tr>
<tr>
<td>Cardiac output</td>
<td>6.0 liters/min</td>
</tr>
<tr>
<td>PVR</td>
<td>1.0 mmHg/l/min</td>
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Exercise (patient only reached 15 Watts on supine ergometer)  
PA pressure rose to 70/40, but with WP 40 mmHg. CO 10.8 lpm, PVR 0.93.

DIAGNOSIS: Heart Failure w/preserved EF (HFpEF; aka, diastolic HF)

TREATMENT: Discontinuation of bosentan, sildenafil. Diuresis.
Case 2

History: 40 y.o. woman with 6 months of progressive dyspnea on exertion. She also reports bouts of exertional lightheadedness and exertional chest tightness. No syncope. No orthopnea, PND. 1+ LE edema persistent over the past month. Dyspnea with mild activity.

PMH: none


Echo: Normal LV size, function. Mild left ventricular hypertrophy. Trace TR: RVSP by Doppler 30 mmHg.
History: 40 y.o. woman with 6 months of progressive dyspnea on exertion. She also reports bouts of exertional lightheadedness and exertional chest tightness. No syncope. No orthopnea, PND. 1+ LE edema persistent over the past month. Dyspnea with mild activity.

PMH: none
Social history: nonsmoker, no drug use.

Look at the ENTIRE echo (preferable)

Or

ENTIRE echo report....
• Normal LA. No LVH. RV appears dilated in this view.
• Note prominent moderator band.
• Dilated coronary sinus.
• SYSTOLIC septal flattening...
- RV:LV ratio >1.0; RA>RA.
- RV apex sharing.
- “open” or rounded RV apical angle.

**TAPSE 1.5 cm**
- Normal RV function: **TAPSE 2.3-2.7 cm**
- Mild RVD: TAPSE 1.9-2.2 cm
- Mod RVD: TAPSE 1.5-1.8 cm
- Severe RVD: TAPSE < 1.5 cm

- RV:LV ratio >1.0; RA>RA.
- RV apex sharing.
- “open” or rounded RV apical angle.
Let’s integrate the echo-Doppler findings….

‘RIGHT’

- Severe RV dysfunction
- RV dilatation (open apical angle)
- + septal flattening
- Normal LA
- No LVH
- Mid-systolic notch Doppler RVOT
- Grade I DD

‘LEFT’
Question:

What is the most appropriate next step in this case?

A. Start sildenafil 40 mg TID
B. Start inhaled Iloprost
C. Diuresis
D. Perform right heart catheterization
E. Perform ventilation perfusion scan

F. D and E are both correct.
### Right heart catheterization

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RA</td>
<td>12 mmHg</td>
</tr>
<tr>
<td>PA</td>
<td>100/40 (60) mmHg</td>
</tr>
<tr>
<td>Wedge pressure</td>
<td>8 mmHg</td>
</tr>
<tr>
<td>Transpulmonary gradient</td>
<td>52 mmHg</td>
</tr>
<tr>
<td>Cardiac output</td>
<td>3.0 liters/min</td>
</tr>
<tr>
<td>PVR</td>
<td>17 mmHg/l/min</td>
</tr>
</tbody>
</table>

**VQ scan very low prob.**

**DIAGNOSIS:** (idiopathic) pulmonary arterial hypertension

**TREATMENT:** Urgent initiation of aggressive PH specific therapy. Diuresis.
Case 3

58 yo man, Family Medicine Physician. Competetive cyclist.

100+ mile rides on the weekends.

Reports difficulty in ‘keeping up with the pack’ on rides

In the last 2 weeks, near syncope while cycling

Exam: 116/82, HR 74, 6’1” 200 lbs. Muscular build. SpO2 96% RA.

JVP 10, AJR
1+ edema

ETCO2 22

6MWD 493 meters
98% SpO2 at end of walk on RA
HR 72→86
Healthy, fit...cyclist.

How bad could it be?
Imaging the lung circulation...
Current and Emerging Treatments for PAH

- Prostacyclin analogs¹
  - IV
  - Inhaled
  - Oral (under development)
- Endothelin-1 receptor antagonists¹
- Phosphodiesterase-5 inhibitors¹
- Combination therapy²

PAH, pulmonary arterial hypertension; IV, intravenous; HMG-CoA, 3-hydroxy-3-methylglutaryl-coenzyme A.
Benefit of PAH Treatment: Meta-analysis

21 RCT conducted 1990-2008
3140 patients
Mean trial duration = 14.3 weeks (range 8-36 weeks)

Mortality (%)

P = .023

Active Treatment
n=1825
1.54%

Placebo
n=1315
3.80%

PAH, pulmonary arterial hypertension; RCT, randomized controlled trials.
ACCF/AHA Consensus PAH Treatment Algorithm

Anticoagulate ± Diuretics ± Oxygen ± Digoxin

Acute Vasoreactivity Testing

Positive

Oral CCB

Sustained Response

No

Lower Risk

ERAs or PDE-5 Is (oral)
Epoprostenol or Treprostinil (IV)
Iloprost (inhaled)
Treprostinil (SC, inhaled)

Yes

Reassess: consider combo-therapy

Investigational Protocols

Negative

Higher Risk

Epoprostenol or Treprostinil (IV)
Iloprost (inhaled)
ERAs or PDE-5 Is (oral)
Treprostinil (SC)

Atrial septostomy
Lung transplant

Summary

• An understanding of PH and its various causes—PH is a heterogeneous condition
  – PAH is a specific form of PH (the details matter…)
  – think like a ‘cardiopulmonologist’…(don’t forget the VQ scan)

• Move ‘beyond the pressure’ in echo-Doppler assessment of PH
  – look for the ‘triad’ of RV dysfunction

• If you suspect PAH→threshold to perform an RHC

• Treatment based on estimate of risk. If unsure of risk assessment or comfort with therapies, low threshold for referral to PH Center…. (happy to help!!).
Getting the diagnosis right

Why it matters...

Baseline PAH diagnosis

2 years later, on PH specific therapy
DOC? CAN YOU WRITE ME A PRESCRIPTION FOR SOME OF THAT VIAGRA?

SAY NO!

THANK YOU