Pulmonary Hypertension Case Studies

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Disclosures

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Pulmonary Hypertension
What is Pulmonary Hypertension?

- Pulmonary Hypertension is increased pressure in the pulmonary arteries.

- Pulmonary Hypertension causes symptoms such as shortness of breath during routine activity (for example, climbing two flights of stairs), tiredness, chest pain, and a racing heartbeat. As the condition worsens, its symptoms may limit all physical activity.

- Pulmonary hypertension (PH) was previously classified into 2 categories: 1) primary pulmonary hypertension; or 2) secondary pulmonary hypertension according to the presence of identified causes or risk factors.

<table>
<thead>
<tr>
<th>PH: WHO Group Classification¹</th>
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</thead>
<tbody>
<tr>
<td>1. PAH</td>
</tr>
<tr>
<td>- Idiopathic PAH</td>
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<tr>
<td>- Familial (heritable) PAH</td>
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<tr>
<td>- Associated with:</td>
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<tr>
<td>- Connective tissue disease</td>
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<tr>
<td>- BMPR2, ALK1, endoglin</td>
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<tr>
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<tr>
<td>- Drugs and toxins</td>
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<tr>
<td>- Other (thyroid)</td>
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<tr>
<td>- Persistent pulmonary hypertension of the newborn</td>
</tr>
<tr>
<td>2. PH associated with left heart disease - Diastolic, Systolic or Valvular disease</td>
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<tr>
<td>3. PH associated with respiratory disease - COPD - Interstitial lung diseases</td>
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<tr>
<td>4. PH due to chronic thrombotic and/or embolic disease</td>
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5. Miscellaneous (sarcoidosis, glycogen storage disease)

PH: WHO Group Classification

1. Pulmonary Venous Hypertension
   - Mitral valve disease
   - Aortic valve disease
   - Systemic hypertension
   - Left ventricular dysfunction
     - Systolic
     - Diastolic
   - Constrictive pericarditis
   - Restrictive cardiomyopathies
   - Various cardiomyopathies

Pulmonary Venous Hypertension: Valvular heart disease (HD)
- Hypertensive HD
- Cardiomyopathies
- Transmitted pressure results in reactive vasoconstriction

Treat primary problem
1. PAH
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   - Familial (heritable) PAH
   - Associated with:
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Lung/Respiratory Diseases Associated with PH

- Obstructive Lung Diseases
  - COPD
  - Asthma
  - Cystic fibrosis
  - Bronchiectasis
  - Bronchiolitis obliterans

- Restrictive Lung Diseases
  - Neuromuscular diseases
  - Kyphoscoliosis
  - Thoracoplasty
  - Sequelae of pulmonary tuberculosis
  - Sarcoidosis
  - Pneumoconiosis
  - Drug-related lung diseases
  - Extrinsic allergic alveolitis
  - Connective tissue diseases
  - Idiopathic interstitial pulmonary fibrosis
  - Interstitial pulmonary fibrosis of known origin

Respiratory Insufficiency of "Central" Origin

- Central alveolar hypoventilation
- Obesity-hypoventilation syndrome
- Obstructive sleep apnea
• Multiple thrombi/emboli
• Can extend into multiple lobar and segmental branches
• Vascular fibrosis and inflammation

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       • Sickle cell disease
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   - COPD
   - Interstitial lung diseases

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PH: WHO Group Classification

1. Simonneau G et al. JACC 2004

Pulmonary Arterial Hypertension (PAH)
What is PAH?

- PAH is a syndrome characterised by a progressive increase in pulmonary vascular resistance (PVR)
  - leads to right ventricular overload
  - eventually leads to right ventricular failure and premature death
  - If untreated, the median survival is 2.8 years which is comparable with some malignancies
- Increased PVR is related to progressive changes in the pulmonary arterioles
  - vasoconstriction
  - obstructive remodelling of the pulmonary vessel wall
  - inflammation
  - in-situ thrombosis
  - Sitbon O et al. Circulation 2005

Survival in PAH

PAH: why does it develop?

- Exact cause of PAH remains unknown
- Endothelial dysfunction occurs early on in the disease process
- Endothelial dysfunction results in
  - reduced production of vasodilators
  - over production of vasoconstrictors
  - endothelial and smooth muscle cell proliferation
  - remodelling of the pulmonary vascular bed and increased vascular resistance

McLaughlin VV et al. Chest. 2004;126:785-92S.
Approved Therapeutic Targets

PAH: why does it develop?

- Reduced production of vasodilators
  - Prostacyclin
    - potent vasodilator
    - potent inhibitor of platelet activation
    - therapy with synthetic forms of prostacyclin may help to correct this deficiency
  - Nitric oxide
    - potent vasodilator
    - possesses anti-proliferative properties
    - vasodilatory effect is mediated by cGMP
    - rapidly degraded by phosphodiesterases

PAH: why does it develop?

- Increased production of vasoactive compounds
  - Endothelin (ET)
    - elevated levels are seen in PAH patients
    - levels correlate with disease severity
    - deleterious effects mediated through endothelin receptors
      - fibrosis
      - hypertrophy and cell proliferation
      - inflammation
      - vasoconstriction
  - endothelin receptor antagonists can block these effects
- Endothelin, nitric oxide and prostacyclin have been the principal focus of research into treatments for PAH.
Pathophysiology of PAH: An Integrated View

Genetic Predisposition

Other Risk Factors

Altered Pathways and Mediators

Proliferation

Thrombosis

Vascular Remodeling

Vasoconstriction

Pathogenesis of Pulmonary Arterial Hypertension

PAH: how common is it?

- PAH is rare
  - an estimated prevalence of 30–50 cases per million
  - most common in young women

- Mean age of diagnosis 36 years

- The prevalence in certain at-risk groups is higher
  - HIV-infected patients (0.50%)
  - sickle cell disease (20–40%)
  - systemic sclerosis (16%)

- True prevalence may be higher

**PAH Related to Connective Tissue Disease**

- Connective tissue diseases
  - scleroderma (most common)
  - systemic lupus erythematosus
  - Sjogren’s syndrome
  - rheumatoid arthritis
  - MCTD

- PH is one of the top causes of death in scleroderma
- Similar to IPAH pathology
- Medical treatment same as for IPAH, but benefits less than for IPAH

[Hachulla E et al. Rheumatology. 2009;48:304-308.]

**Survival in Pulmonary Arterial Hypertension**

- Survival rates (patients with IPAH) at 1, 3 and 5 years were 68%, 48% and 34% respectively
- PAH mortality contributed to
  - Right heart failure 47%
  - Sudden Death 26%
  - Other (pneumonia) 27%

- Although new treatments have improved mortality rates, there is little evidence to support reversal of aberrant remodeling


**Schematic Progression of PAH**

![Schematic Progression of PAH](image)
Diagnosis of Pulmonary Arterial Hypertension (PAH)

**Signs of PAH on Electrocardiogram (ECG)**

- RVH: Right ventricular hypertrophy
- RAE: Right atrial enlargement
- RV strain

**Signs of PAH on Chest X-ray**
PAH: Early diagnosis is crucial

- If untreated, the median survival is 2.8 years which is comparable with some malignancies12
  - diagnosis can be delayed for months or years and frequently occurs when disease is relatively advanced4
  - mean time from onset to diagnosis is estimated to be approximately 2 years5

- Although patients progress at different rates; early stage PAH is still a devastating condition and can rapidly deteriorate
  - Early diagnosis and intervention is therefore crucial
  - patients who begin targeted therapy in less severe PAH (WHO FC1/2) demonstrate a better prognosis than those in a more severe stage (WHO FC3/4)6

Screening Patients With Symptoms

- Echocardiogram
  - High clinical suspicion based on clinical exam, etc
  - CTD (Systemic Sclerosis (SSc), Lupus, RA, Scleroderma)
  - Liver transplant candidates
  - Shunts
  - Amphetamine Derivatives
  - Family members of a patient with familial Pulmonary Arterial Hypertension (FPAH)
  - Patients with HIV

- PFT's
- Polysomnography
- VQ Scan
  - Sleep Disorder
  - Chronic PE

- Functional Test (6MWT, CPET)
  - Overnight Oximetry

- HIV
- ANA
- LFT's
- RH Cath
- TEE
- Exercise Echo
- Pulmonary Angiography
- Chest CT Angiogram
- Coagulopathy Profile
- Vasodilator Test
  - Exercise RH Cath
  - Volume Loading

- ABG's
  - Index of Suspicion of PH
  - RVE, RAE, RVSP, RV Function
  - Left Heart Disease
  - VHD, CHD
  - Ventilatory Function
  - Gas Exchange

- Other CTD Serologies
  - HIV Infection
  - Scleroderma, SLE, RA
  - Portopulmonary Htn

- Establish Baseline
  - Prognosis
  - Confirmation of PH
  - Hemodynamic Profile
  - Vasodilator Response

- Contingent Tests
  - Contribute to Assessment of:
    - Left Heart Cath
    - CXR
    - ECG

VQ Scan


Contingent Tests

Pivotal Tests

History

Exam

PV= 4(V_2)^2 + RAP

3-4% of acute PE do not entirely resolve

½ of those with CTEPH do not have an apparent history of acute PE

Normal or very low probability VQ essentially excludes chronic PE

CTEPH should be excluded, even when another explanation for PH is present
Minimize spontaneous variability >25 mm Hg; only 2 had Right atrial pressure take measurements over 2

17% (37/220) of patients with OSA have daytime mPAP >20 mm Hg; 16 had mPAP >25 mm Hg; only 2 had mPAP >35 mm Hg
Marked ↑ with sub-max exercise (mean mPAP 47 mm Hg) – in part due to ↑ PCWP
Contributing factors: obesity, hypoxemia, COPD

In patients with OSA, JAP reported in response to CPAP therapy

Untreated – response to other treatment likely less effective

- Oxygen saturations (SVC, IVC, PA, SA)
- Right atrial pressure
- RV systolic and end-diastolic pressure
- PA systolic, diastolic, and mean pressure
- PVAP, LVEDP, or LAP
- Thermodilution or Fick CO, CI
- Pulmonary vascular resistance
- Systemic systolic, diastolic, and mean pressure
- Heart rate
- Vasodilator response

Vasodilator response
- iNO recommended
- decrease in mPAP by ≥10 mm Hg
- Decrease of mPAP to ≤40 mm Hg
- rare in scleroderma, hereditary, diet-pill-induced
- risk of pulmonary edema with left heart disease or PVOD
- RHC is safe (1.1% serious events)
- hematoma, pneumothorax, arrhythmias, hypotension
- Minimize spontaneous variability
- take measurements over 2-3 respiratory cycles at end-expiration
Hemodynamic Definition of PH/PAH

**PH**
Mean PAP ≥ 25 mm Hg

**PAH**
Mean PAP ≥ 25 mm Hg plus
PCWP/LVEDP ≤ 15 mm Hg

What is the Optimal Treatment Strategy?

<table>
<thead>
<tr>
<th>Anticoagulate ± Diuretics ± Oxygen ± Digoxin</th>
</tr>
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<tbody>
<tr>
<td>Vasodilator Study</td>
</tr>
<tr>
<td>Positive</td>
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<tr>
<td>Oral CCB</td>
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<tr>
<td>Sustained Response</td>
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<tr>
<td>Lower Risk</td>
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<tr>
<td>Determinants of Risk</td>
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<tr>
<td>Higher Risk</td>
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<tr>
<td>Yes</td>
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<tr>
<td>No</td>
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<tr>
<td>Clinical Evidence of RV Failure</td>
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<td>Yes</td>
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<td>No</td>
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<td>Progression</td>
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<td>Rapid</td>
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<td>NYHA Class</td>
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<tr>
<td>IV</td>
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<tr>
<td>Exercise Test</td>
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<tr>
<td>More than 90%</td>
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<tr>
<td>Radically increased</td>
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<tr>
<td>200–300 m</td>
</tr>
<tr>
<td>Very exerted</td>
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<tr>
<td>100–200 m</td>
</tr>
<tr>
<td>Minimally elevated</td>
</tr>
<tr>
<td>Echocardiographic Findings</td>
</tr>
<tr>
<td>Sustained RV Dysfunction</td>
</tr>
<tr>
<td>Hemodynamics</td>
</tr>
<tr>
<td>Normal/Near normal</td>
</tr>
<tr>
<td>High RAP, Low CI</td>
</tr>
</tbody>
</table>

Goal-Oriented Therapy

**Diagnosis of PAH**
Vasoreactivity test negative
NYHA II or IV

Baseline examination and 2- to 6-month evaluation to assess treatment goals
(6MWD > 380 m, peak VO2 > 10.4 mL/min/kg, peak systolic BP > 120 mm Hg during exercise)

Treatment goals not met
First-line treatment ERA
Addition of PDE-5 inhibitors
Addition of oral or inhaled prostanoid
Transition from inhaled to IV/SQ prostanoid
Highly urgent lung transplantation

Adapted from Hauser et al. Eur Respir J. 2005;26:584-590
Case Study

DE is a 66 year old male who presented to his primary care physician's office with complaints of cough, increased fatigue and dyspnea on exertion. Past medical history includes hypertension, smoking and osteoarthritis. He had a recent Cardiolite stress test which was negative. BP in office is 160/90. An echocardiogram was ordered.

Height 64 inches. Weight 275 lbs.

Physical Exam: III/VI SEM, 1+ lower extremity edema

Case Study

2D Echo results:

LVEF: 65%
Normal RV function
Stage I diastolic dysfunction
Mild LVH
Mild biatrial chamber size enlargement
Normal left and right ventricular size
Severe tricuspid regurgitation
RVSP 60 mmHg
Case Study

Based on the initial presentation and echocardiogram your next step would be as follows?
BP in office is 160/90. Weight 275 lbs.

A. No further testing or treatment is indicated  
B. Start on oral diuretics  
C. Set up for a PFT, VQ Scan and Sleep Study  
D. Place on anti-hypertensive medications  
E. Referral to TCI Cardiology

Case Study

You decided to place DE on HCTZ 25 mg and lisinopril 5 mg daily. He returns one month later with continued dyspnea. BP in office is improved at 138/80. An ECG was performed which was essentially normal. He denies CP.

Height 64 inches. Weight 220 (225) lbs.  
Physical Exam- III/VI SEM, 1+ lower extremity edema

Case Study

Given his continued symptoms, what would be your next step?

A. No further testing or treatment is indicated  
B. Refer to weight loss management center  
C. Set up for a PFT, VQ Scan and Sleep Study  
D. Increase anti-hypertensive medications  
E. Referral to TCI Cardiology
Case Study

Comprehensive Evaluation

Review previous echocardiograms
Pulmonary Function Study with DLCO
Apnea Link Monitor / Sleep study
VQ Scan
Labs- ANA, RF (if no history of CTD), BNP, LFT’s, TSH, HIV
Echo with saline contrast r/o shunt
BP logs
6MWT

Case Study

Severe Obstructive Sleep Apnea/Stage I diastolic dysfunction

Other studies normal.
CPAP for 3 months then re-evaluate
Blood pressure control
6MWT
2D echo limited check RVSP

• 17% (37/220) of patients with OSA have daytime mPAP >20 mm Hg
  - 16 had mPAP >25 mm Hg; only 2 had mPAP >35 mm Hg
  - Marked ↑ with sub-max exercise (mean mPAP 47 mm Hg) – in part due to ↑ PCWP
  - Contributing factors: obesity, hypoxemia, COPD

• In patients with OSA, ↓PAP reported in response to CPAP therapy

• Untreated – response to other treatment likely less effective
Case Study

HG is a 62 year old female who presented to your office for a hospital follow up after not having been seen for 4 years. She has a known history of HTN, hyperlipidemia and fibromyalgia. She was recently hospitalized for shortness of breath and underwent an echocardiogram which demonstrated an EF of 35% with no significant valvular abnormalities. A catheterization was performed which demonstrated normal coronaries and a PCWP of 23 mmHg (normal 8-10 mmHg) with a mPAP of 30 mmHg (normal 12-15 mmHg). She was diagnosed with a non ischemic CM and placed on medical therapy. Her echocardiogram demonstrated an RVSP of 65 mmHg.

Height 66 inches. Weight 165 lbs.
Physical Exam- III/VI SEM, 1+ lower extremity edema

Case Study

2D Echo results:
LVEF: 35%
Normal RV function
Stage I diastolic dysfunction
Mild LVH
Mild biatrial chamber size enlargement
RVSP 65 mmHg

Case Study

Based on her hospitalization and echocardiogram with abnormal RVSP what would be her diagnosis?

A. Pulmonary Arterial Hypertension
B. PH WHO Group II secondary to LH disease
C. PH WHO Group III secondary to Intrinsic lung disease
D. CTEPH
E. More information is needed to make this diagnosis
Case Study

JB is a 68 year old female who presented for routine follow up for atrial flutter. Routine echo performed for mild MR after 3 years demonstrated NL EF, mild MR, Mod to Severe TR, possible Mild right atrial enlargement. RVSP 56 mmHg (moderate pulmonary hypertension) without other significant findings. She is asymptomatic. No SOB or chest pain. Past Medical History includes HTN and Paroxysmal A. Flutter. Currently in NSR. On warfarin and lisinopril only.

Height 64 inches. Weight 135 lbs. BP 130/80
Physical Exam- Normal

Case Study

2D Echo results 03/2014:
- Normal left and right ventricular function with an LVEF of 64%.
- Normal wall motion of all segments at rest.
- Subjectively the right ventricle appears upper limits of normal and both atrium appear mildly dilated although measure normal as viewed.
- Mild mitral valve regurgitation.
- Moderate to severe tricuspid valve regurgitation.
- Tissue Doppler consistent with normal left atrial pressure.
- Moderate pulmonary hypertension.
- No pericardial effusion seen.
- RVSP 56 mmHg

Case Study

2D Echo results 2010:
- Normal left ventricular function with an EF of 55%.
- Moderate biatrial enlargement.
- Mild right ventricular enlargement.
- Moderate mitral valve regurgitation.
- Mild tricuspid valve regurgitation.
- Mild pulmonary hypertension.
- RVSP 49 mmHg
Case Study

Based on her presentation and reviewing the previous echocardiograms your next step would be as follows?

A. No further testing or treatment is indicated
B. Recommend a CT of her chest
C. Set up for a PFT, VQ Scan and Sleep Study
D. Place on anti-hypertensive medications
E. Referral to TCI Cardiology

Case Study

Given abnormal chamber size and dimensions with increased RVSP recommended PFT, VQ and Sleep Study

Comprehensive Evaluation

Pulmonary Function Study with DCLO- Air trapping consistent with airflow obstruction. Severely impaired diffusion.

Apnea Link Monitor / Sleep study= negative
VQ Scan= negative
Labs= negative
Echo with saline contrast r/o shunt= negative

COPD and PH

• Retrospective study of 215 COPD patients
• 13% had a PA mean >35 mm Hg
• Correlated best (inversely) with PaO2
• A small number had only moderate obstruction: treatable sub-group?

Case Study
VG is a 43 year old female who presented with lower extremity swelling and dyspnea on exertion which has been worsening over the last 6 months. 2D echocardiogram demonstrated an RVSP of 71 mmHg. Known history of Scleroderma. 30 plus pack year smoking history. No history of CAD with recent negative stress test.

2014 2D Echo results:
LVEF: 55%
Reduced RV function
Mild bialtrial chamber size enlargement
Mild right ventricular enlargement
Severe tricuspid regurgitation
RVSP 71 mmHg
2007 Echo- Normal LV and RV function RVSP- 34 mmHg

Case Study
Based on her presentation and reviewing the previous echocardiograms your next step would be as follows?
A. No further testing or treatment is indicated
B. Place patient on sildenafil therapy
C. Set up for a PFT, VQ Scan and or a Sleep Study
D. Refer to Rheumatology
E. Referral to TCI Cardiology

Diagnostic Confirmation: Right Heart Catheterization
In patients with suspected PAH:
• Right heart catheterization is required to confirm the presence of PAH, establish the specific diagnosis and determine the severity
  [Strength of recommendation: A]
• Right heart catheterization is required to guide therapy
  [Strength of recommendation: B]
Right heart catheterization: the diagnostic gold standard

**Definitions**

RAP is defined by:
- $\text{RAP} > 20$ mmHg
- $\text{RAP} > 30$ mmHg at rest
- $\text{RAP} > 15$ mmHg with exercise
- $\text{RAP} > 3$ units

Cardiac output is also required to calculate PCWP.

**Right heart catheterization**

- RHC should always assess
  - right atrial pressure (RAP)
  - systolic, diastolic and mean pulmonary arterial pressure (PAP)
  - pulmonary capillary wedge pressure (PCWP)
  - cardiac output / index
  - PVR and systemic vascular resistance
  - blood pressure and arterial and mixed venous oxygen saturation

- RHC can assess vasoreactive response
  - shown in only 10–15% of patients
  - sustained response is shown in less than 7% of patients

Case Study

Right Heart Catheterization

RA-8 mmHg
mPAP- 49 mmHg
PCWP- 4 mmHg
Transpulmonary gradient-45 mmHg
Cardiac output- 5.13 l/min
PVR-8.775 woods units
Negative Vasodilator challenge

Case Study

VT is a 26 year old female who presented to her primary care physicians office in February 2010 with complaints of cough, increased fatigue and significant dyspnea on exertion. Otherwise healthy female, no significant past medical history, has one healthy child. No findings were noted on her physical exam. She was given Singulair and albuterol MDI and recommend follow up in 1 week. She continued to have SOB and she proceeded to the ER on day three.

During her ER visit an ECG was ordered. All labs were normal. CXR performed and ER notes no significant findings.
Case Study

What is the main abnormality on the EKG?

A. ST Segment Depression
B. Right Ventricular Hypertrophy
C. Left Ventricular Hypertrophy
D. Right Bundle Branch Block
E. Left Bundle Branch Block

Case Study

Patient was discharged from ER to follow up with PCP. Patient was lost to follow up until September 2010 when she was seen at her PCP with continuing shortness of breath. An Echocardiogram was ordered.

A consultation was requested with Pulmonary Services and seen in October.

Case Study

(Additional medical information and diagrams related to the case study)
Case Study

Based on her presentation and reviewing the previous echocardiograms your next step would be as follows?

A. No further testing or treatment is indicated
B. Place patient on sildenafil therapy
C. Set up for a PFT, VQ Scan and or a Sleep Study
D. Start her on albuterol and atrovent nebulizer
E. Referral to TC Cardiology

Case Study

Cardiology consult was requested and was seen in November.

Right heart catheterization was performed within a few days which demonstrated a mean pulmonary artery pressure of 64 mmHg consistent with severe pulmonary hypertension.

Early Recognition and Treatment of PAH is Essential

Prognosis of untreated PAH is poor, even when mildly symptomatic (WHO FC II)

<table>
<thead>
<tr>
<th>Condition</th>
<th>Median Survival (years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Functional class I-II</td>
<td>4.9 years</td>
</tr>
<tr>
<td>Ovarian cancer</td>
<td>2.6 years</td>
</tr>
<tr>
<td>Functional class III</td>
<td>6 months</td>
</tr>
<tr>
<td>Advanced breast cancer</td>
<td>6 months</td>
</tr>
<tr>
<td>Advanced lung cancer</td>
<td>6 months</td>
</tr>
</tbody>
</table>
Would Earlier Treatment Be Better?

**EARLY Study**


- **Time (wk)**: 0, 25, 50, 75, 100
- **Patients with no clinical worsening (%)**
  - Bosentan (n=80)
  - Placebo (n=88)

- **p = 0.0114**

![Graph showing % patients with no clinical worsening](image)

**What is the Optimal Treatment Strategy?**

Anticoagulate ± Diuretics ± Oxygen ± Digoxin

- **Oral CCB**
  - Positive
  - Negative

- **Sustained Response**
  - Yes
  - Continue CCB

<table>
<thead>
<tr>
<th>Lower Risk</th>
<th>Determinants of Risk</th>
<th>Higher Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>Clinical Evidence of RV Failure</td>
<td>Yes</td>
</tr>
<tr>
<td>No</td>
<td>Progression Rapid</td>
<td></td>
</tr>
<tr>
<td>RVH</td>
<td>NYHA Class IV</td>
<td></td>
</tr>
<tr>
<td>Left ventricular volume overload</td>
<td>6 Minute Walk Distance Shorter (&lt;300 m)</td>
<td></td>
</tr>
<tr>
<td>Minimally elevated</td>
<td>BNP</td>
<td>Very elevated</td>
</tr>
<tr>
<td>Sustained RV dysfunction</td>
<td>Echocardiographic Findings</td>
<td>Papillary Ejection Fraction</td>
</tr>
<tr>
<td>Normalized normal RAP and CI</td>
<td>Hemodynamics</td>
<td>High RAP, Low CI</td>
</tr>
</tbody>
</table>

McLaughlin VV and McGoon M. Circulation. 2006;114:1417-1431

**Collaborative Care With PH Centers:**

- Local Care
  - Diagnostic dilemmas
  - Diagnostic cath
  - Vasodilator trial
  - Fluid management
  - Acute issues
  - PAH-specific therapies
  - Side effects
  - Hospitalizations
  - Transplant
  - Clinical trials

- PH Center
Final Thoughts

- Comprehensive history and physical is foundation for diagnosis
- Noninvasive screening as indicated
- Treat any identified factor(s) that could contribute to or exacerbate pulmonary hypertension
- Invasive hemodynamics are crucial
- Refer early

Thank You for your attention!

References

- Galie N et al. Circulation 2005
- Galie N et al. Eur Heart J 2004
- Bando R et al. J Am Coll Cardiol 2004
- Simonneau G et al. J Am Coll Cardiol 2004
- Gaine S et al. Am J Respir Crit Care Med 2004
- Peacock AJ. BMJ 2003
- Channick RN et al. Am J Respir Crit Care Med 2003
- McGoon M et al. Chest 2004
- Vlachopoulos C et al. J Rheumatol 1994
- Yandle TG et al. Circulation 1991
- Channick RN et al. Lancet 2001
- Kshet्रi et al. Cancer 2001
- Spence JD et al. Am J Respir Crit Care Med 1998
- Gaine S et al. J Am Coll Cardiol 2002