# EVALUATION OF THE PULMONARY HYPERTENSION PATIENT

Navin Rajagopalan, MD
Assistant Professor of Medicine
University of Kentucky
Director, Congestive Heart Failure
Medical Director of Cardiac Transplantation

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# DEFINITION OF PH

- Pulmonary hypertension
  - Mean PAP ≥ 25 mm Hg
- Pulmonary arterial hypertension (PAH)
  - Mean PAP ≥ 25 mm Hg AND
  - Pulmonary capillary wedge pressure/LVEDP ≤ 15 mm Hg

# DEFINITION OF PH

- No easy bedside measure of PH
- Echocardiography can only estimate pulmonary artery systolic pressure
- Confirmation requires right heart catheterization, i.e. Swan-Ganz

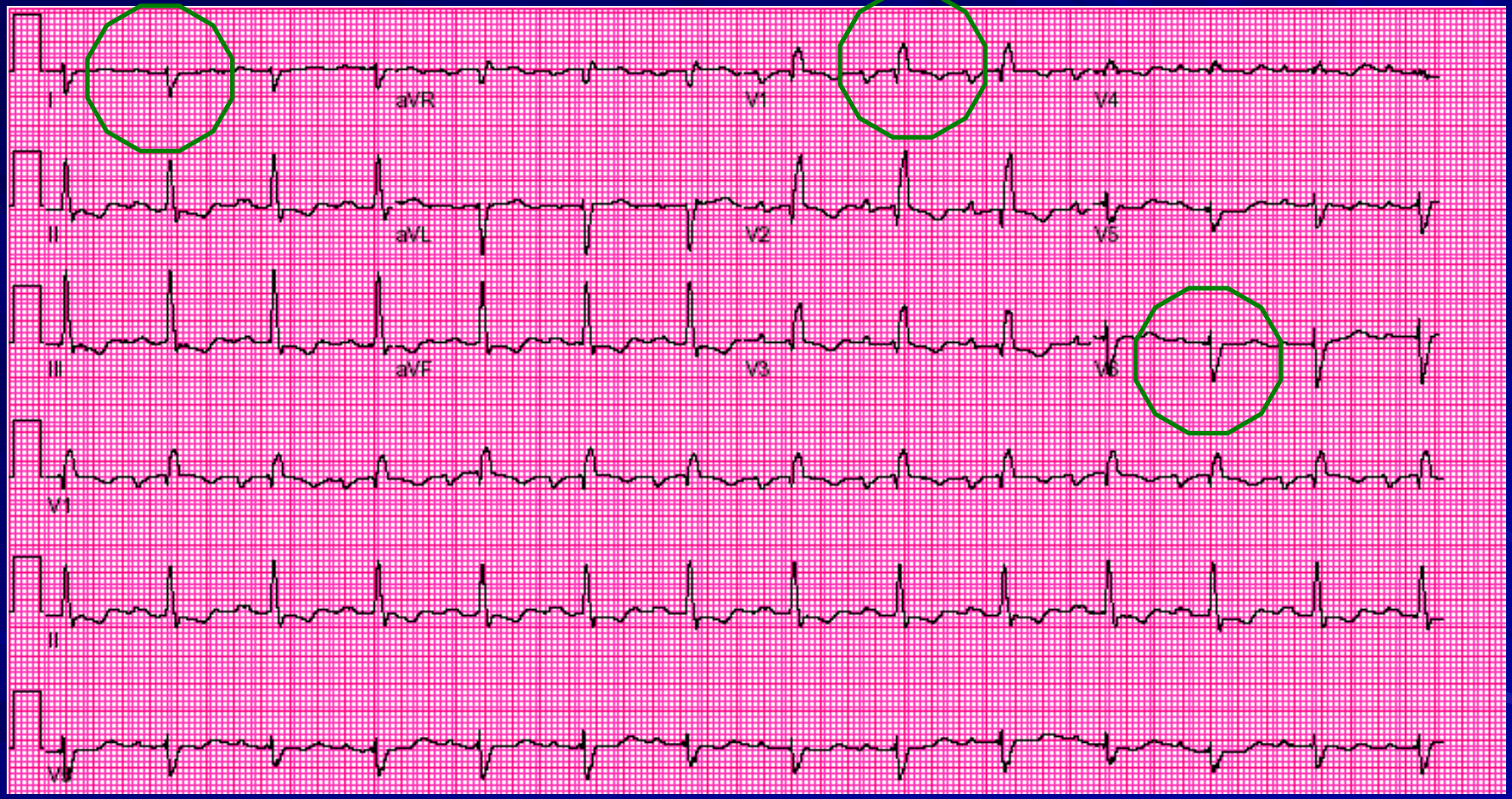
# WHEN TO SUSPECT PH?

- Initial signs and symptoms
  - Dyspnea
  - Dizziness
  - Fatigue
  - Edema
  - Syncope
- Non-specific nature of complaints can lead to confusion with other conditions (CAD, heart failure, asthma, other pulmonary disease)

# PHYSICAL EXAM FINDINGS

- RV lift
- Increased intensity of P2
- Significant TR murmur
- Or NONE!

# ELECTROCARDIOGRAM



# COMMON PATIENT SCENARIO

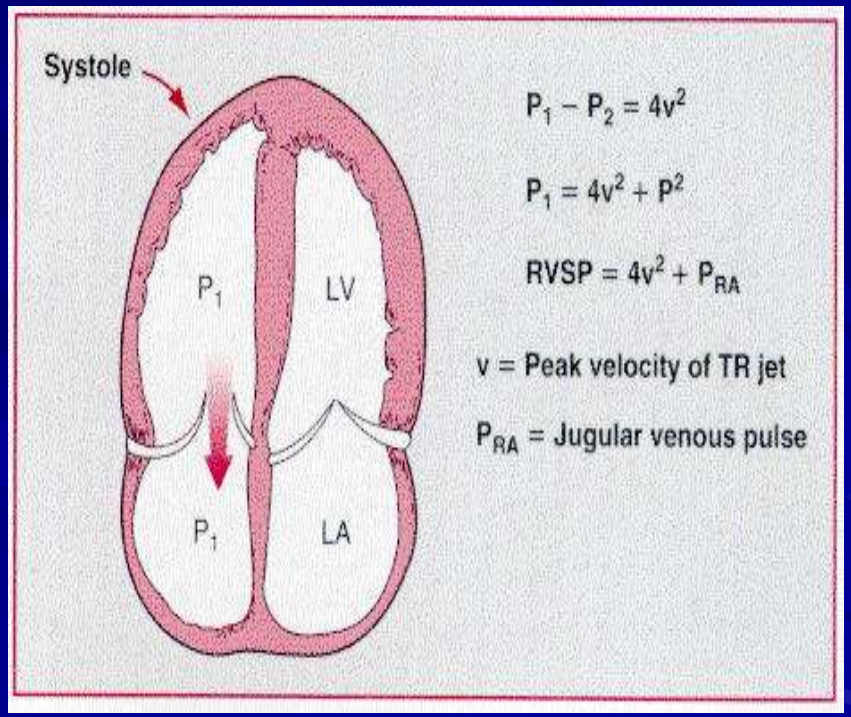
- 58 year old with history of HTN, nicotine dependence presents with 2-3 month history of worsening SOB
- PE: nonrevealing
- Echocardiogram obtained:
  - Normal LV function
  - Normal RV function
  - “Estimated pulmonary artery pressure is elevated at 68 mm Hg”
- What to do next?

# PROBLEMS WITH ECHOCARDIOGRAPHY

- Definition of PH depends upon mean PAP and/or PVR both of which cannot be determined with echocardiography
- Echo can only estimate pulmonary artery systolic pressure (PASP) based upon tricuspid regurgitation velocity
- Cannot determine pulmonary capillary wedge pressure (PCWP)

# IS THE ECHO CORRECT?

- Echocardiography is notorious for overestimating pulmonary artery pressures
- Tricuspid regurgitation signal may be faint or unobtainable
- Sometimes it is better not to report the estimated PA pressures!



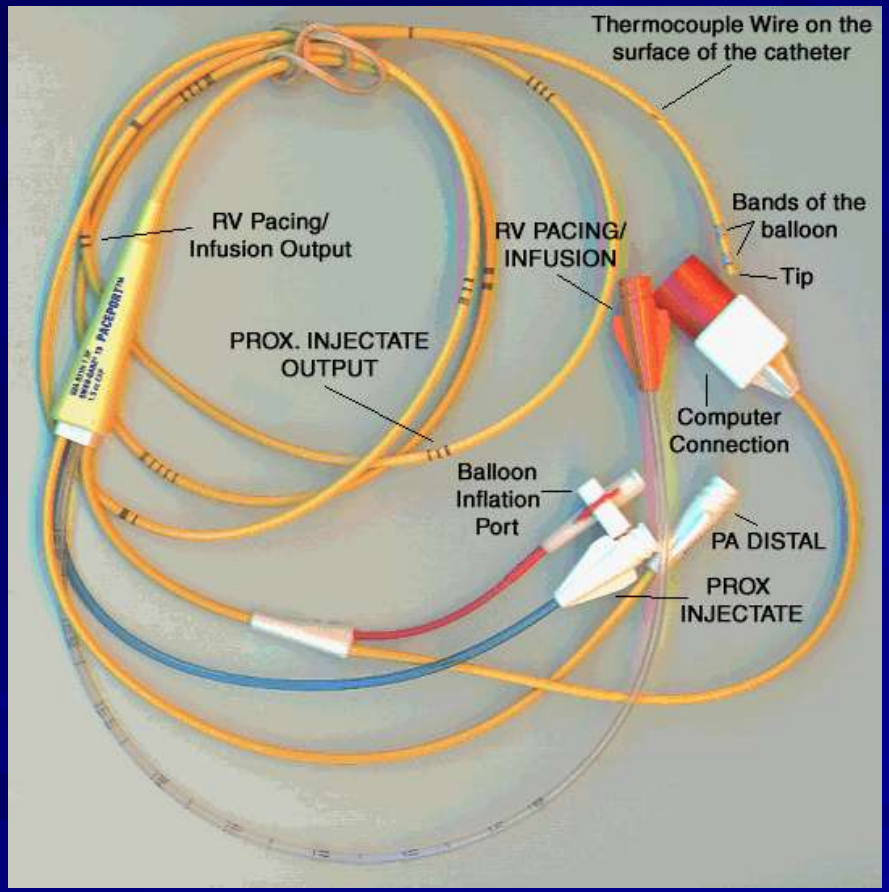
# ECHOCARDIOGRAPHY SUPPORTING EVIDENCE

- Abnormal right ventricular size and/or function
- Enlarged right atrium
- Valvular pathology
  - Mitral regurgitation
  - Mitral stenosis
- Is the left ventricular function normal?

THE ECHOCARDIOGRAM CANNOT MAKE THE DIAGNOSIS OF PULMONARY HYPERTENSION!!

RIGHT HEART CATHETERIZATION IS REQUIRED

# SWAN GANZ CATHETER




- Typically inserted via RIJ or femoral vein
- +/- conscious sedation
- Procedure itself takes 15-30 minutes
- No dye
- Less risk than left heart cath

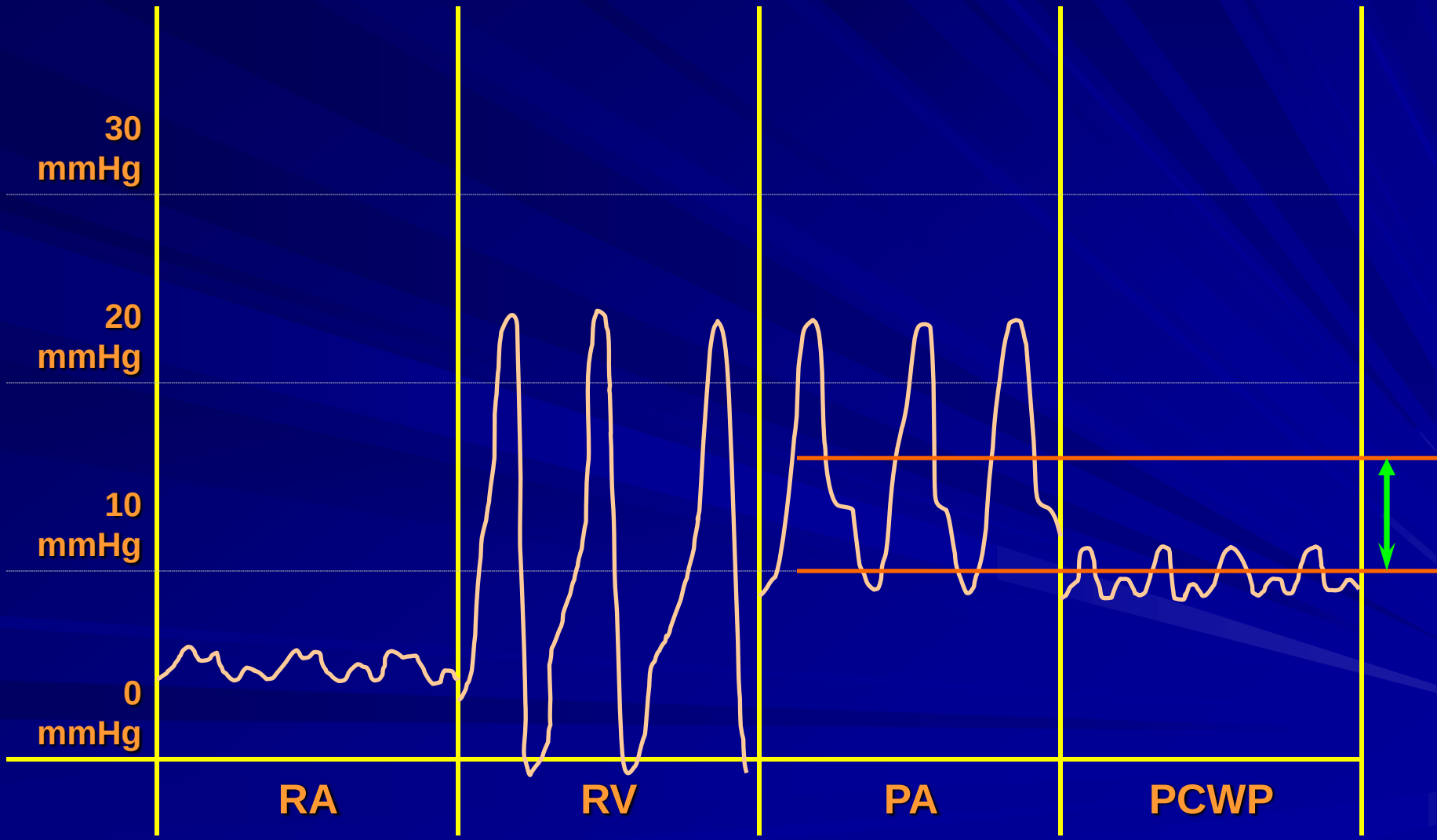
# RIGHT HEART CATHETERIZATION

- Gold standard for diagnosis of PH
- Required before starting therapy
- Careful assessment of PCWP, cardiac output mandatory
  - Determining PCWP can be challenging
- Low risk
  - Bleeding
  - Pneumothorax
- Outpatient procedure

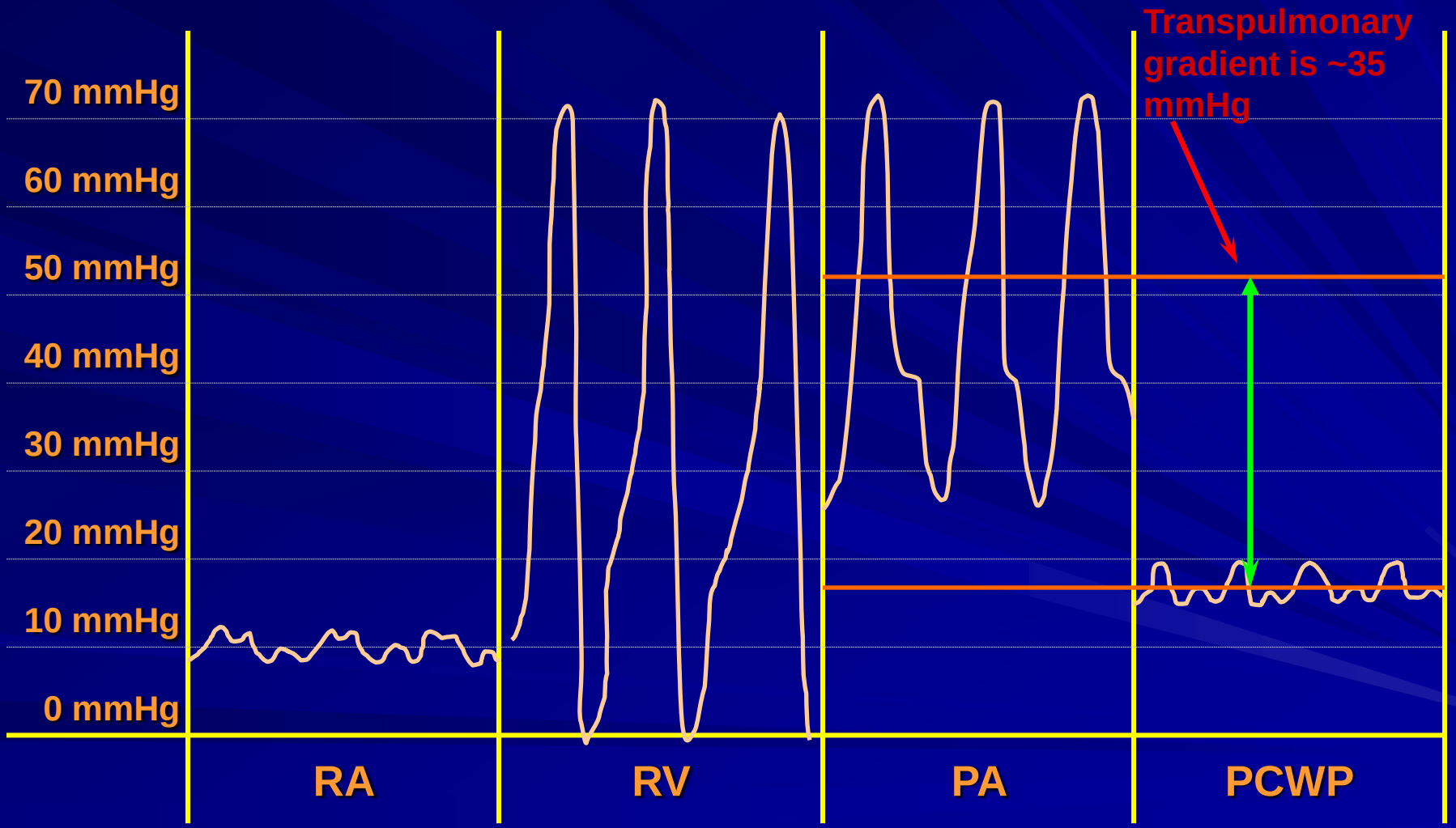
# DO ALL PATIENTS NEED CATH?

- Symptoms
- Risk factors
  - Does patient have systemic disease that puts them at risk for PH?
- How severe is the PH?
  - PASP < 30 mm Hg: Normal
  - PASP 30-40 mm Hg: Likely normal
  - PASP 40-50 mm Hg: May be abnormal
  - PASP > 50 mm Hg: Likely abnormal

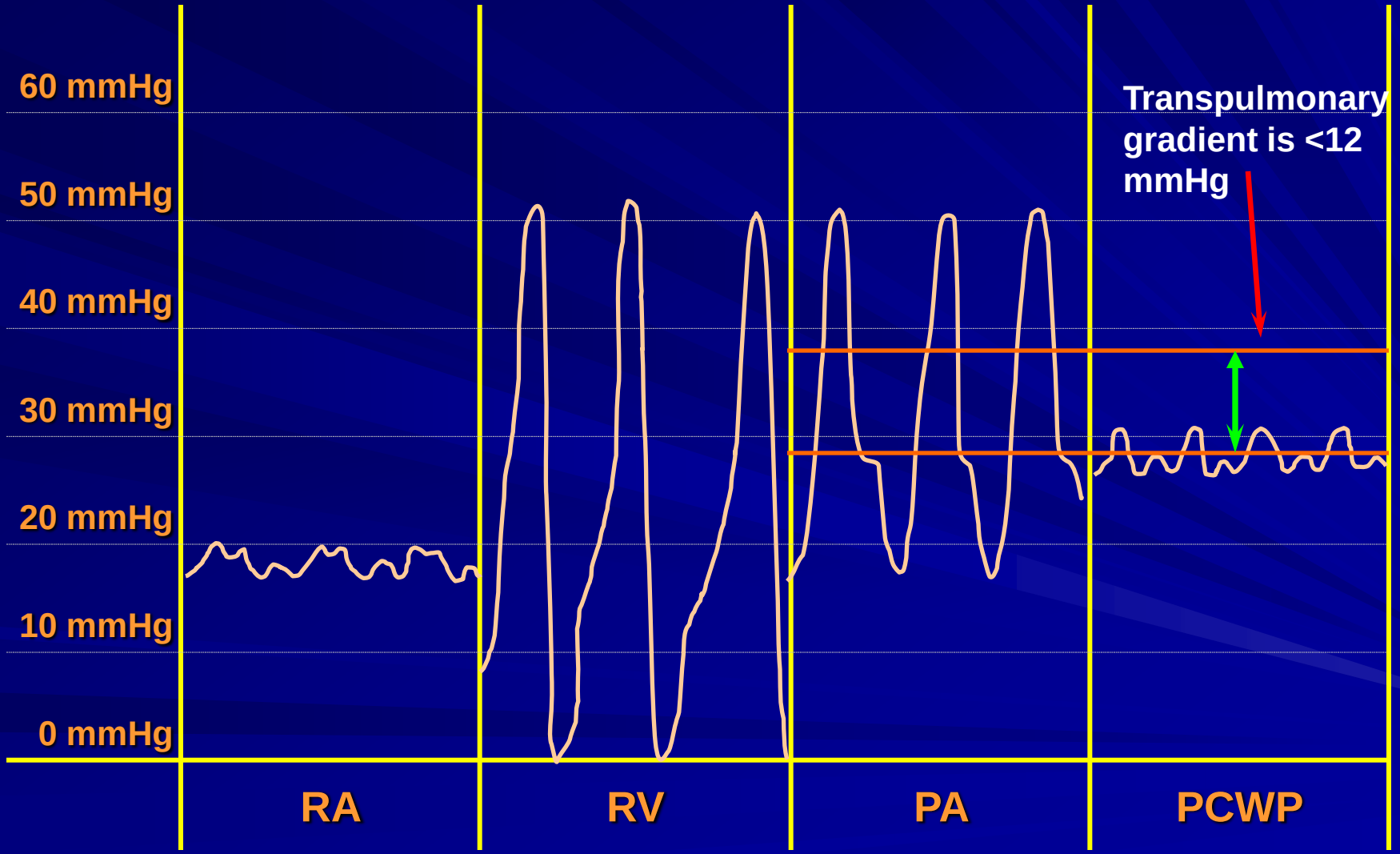
# NORMAL RIGHT HEART CATH



# RIGHT HEART CATHETERIZATION IN PH



# RIGHT HEART CATHETERIZATION IN LEFT HEART DISEASE



# WHY IS THIS IMPORTANT?

- PH-specific therapies have only shown benefit in patients with normal wedge pressure (PCWP) and normal LV function

- If either is abnormal, treatment is limited to treatment of underlying condition (heart failure)

# CLINICAL CLASSIFICATION OF PH

**Table 2** Updated Clinical Classification of Pulmonary Hypertension (Dana Point, 2008)

1. Pulmonary arterial hypertension (PAH)
1.1. Idiopathic PAH
1.2. **Heritable**
1.2.1. **BMPR2**
1.2.2. **ALK1, endoglin (with or without hereditary hemorrhagic telangiectasia)**
1.2.3. **Unknown**
1.3. Drug- and toxin-induced
1.4. Associated with
1.4.1. Connective tissue diseases
1.4.2. HIV infection
1.4.3. Portal hypertension
1.4.4. Congenital heart diseases
1.4.5. **Schistosomiasis**
1.4.6. **Chronic hemolytic anemia**
1.5 Persistent pulmonary hypertension of the newborn

1′. **Pulmonary veno-occlusive disease (PVOD) and/or pulmonary capillary hemangiomatosis (PCH)**

2. Pulmonary hypertension owing to left heart disease
2.1. **Systolic dysfunction**
2.2. **Diastolic dysfunction**
2.3. Valvular disease

3. Pulmonary hypertension owing to lung diseases and/or hypoxia
3.1. Chronic obstructive pulmonary disease
3.2. Interstitial lung disease
3.3. **Other pulmonary diseases with mixed restrictive and obstructive pattern**
3.4. Sleep-disordered breathing
3.5. Alveolar hypoventilation disorders
3.6. Chronic exposure to high altitude
3.7. Developmental abnormalities

4. **Chronic thromboembolic pulmonary hypertension (CTEPH)**

5. **Pulmonary hypertension with unclear multifactorial mechanisms**
5.1. **Hematologic disorders: myeloproliferative disorders, splenectomy**
5.2. **Systemic disorders: sarcoidosis, pulmonary Langerhans cell histiocytosis:** lymphangioleiomyomatosis, neurofibromatosis, vasculitis
5.3. **Metabolic disorders: glycogen storage disease, Gaucher disease, thyroid disorders**
5.4. **Others: tumoral obstruction, fibrosing mediastinitis, chronic renal failure on dialysis**

Simonneau et al. JACC 2009;54: S43-54

# CLINICAL CLASSIFICATION OF PH DANA POINT 2008

- 1. PAH
  - Idiopathic
  - Drugs/toxins
  - Connective tissue disease
  - Congenital heart disease
  - Portal hypertension
- 2. PH due to left heart disease
  - Systolic/diastolic dysfunction
  - Valvular heart disease
- 3. PH due to chronic lung disease
- 4. PH due to chronic thromboembolic disease
- 5. PH due to miscellaneous
  - Sarcoidosis

# PROBLEM WITH CLASSIFICATION SYSTEM

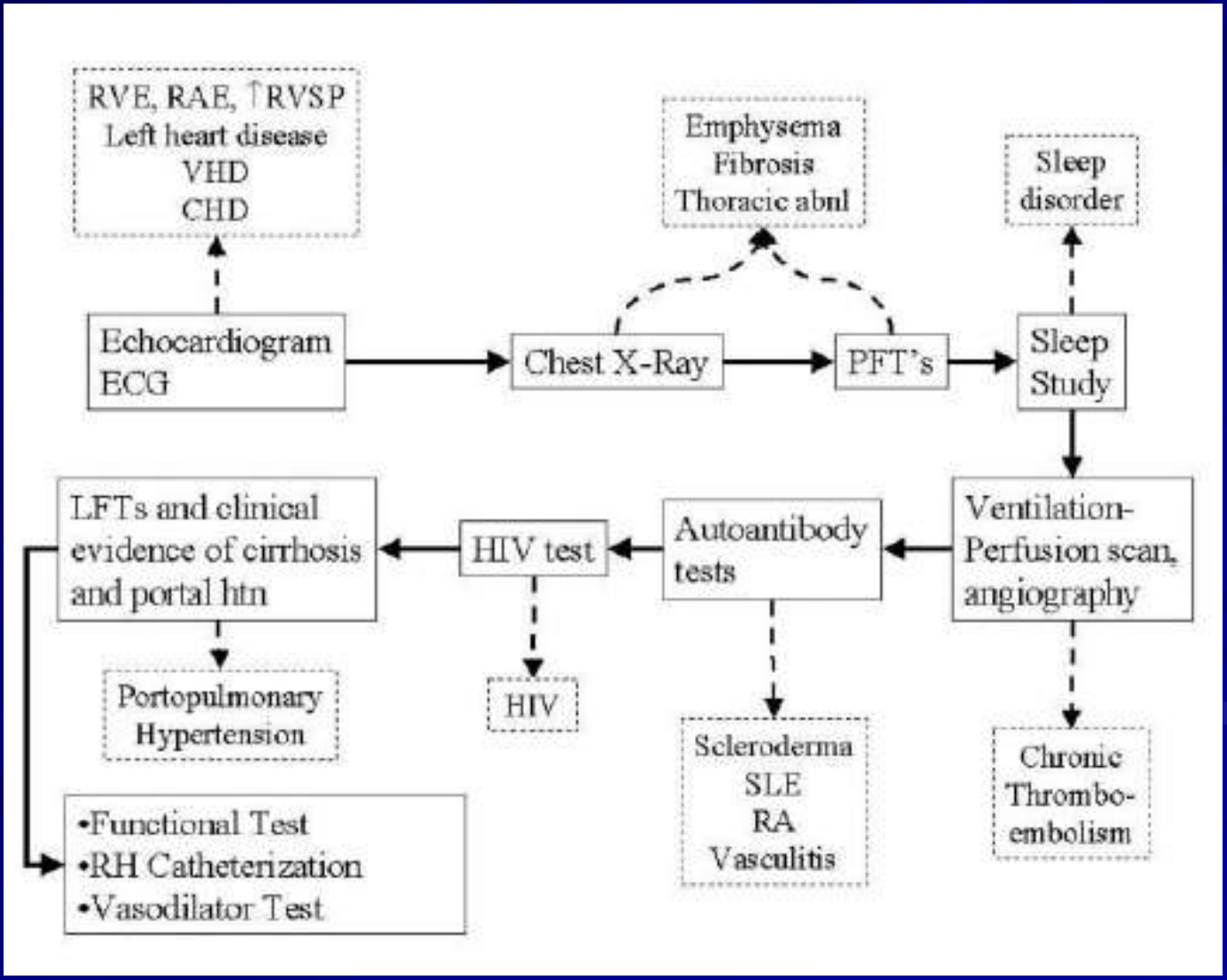
- Does not account for patients with known heart/lung disease who also develop PH

- Many patients will have mixed picture
  - Elevated PA pressures; elevated wedge pressure; risk factors for both diastolic heart failure AND lung disease

# WHAT IS THE CAUSE OF PH?

- Echocardiogram
  - LV function: normal
  - Valvular heart disease: MR, MS
  - How does the RV look?
- Chest CT
- PFTs
- V/Q scan
  - Better than contrast CT for chronic, smaller PE
- Basic rheumatologic work-up
- HIV
- Liver disease
- Sleep study

# WHAT IS THE CAUSE OF PH?




McLaughlin et al. Circ 2006;114:1417-31

# PH AND LEFT HEART DISEASE (GROUP 2)

- Most common type of PH that you will experience in clinical practice
- Related to chronic elevation in LVEDP which results in chronic elevation in pulmonary artery pressures
- PH can develop “out of proportion” to left heart disease
- Not well studied (trials excluded patients with elevated PCWP)
- Co-existing comorbidities often present

# PH DUE TO LEFT HEART DISEASE

**Table 1** Risk Factors Favoring Diagnosis of Diastolic Heart Failure

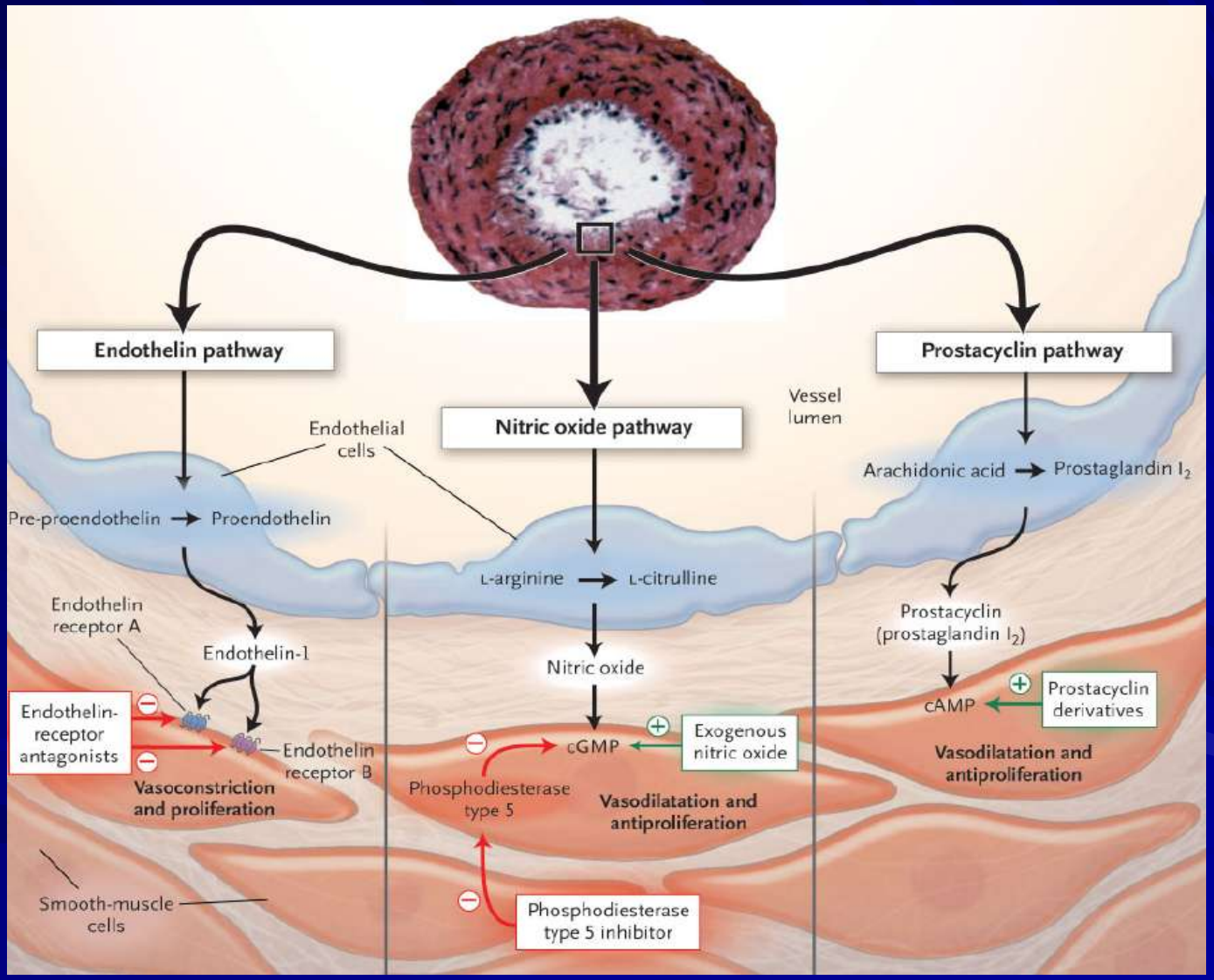
| |
|---|
| Clinical features |
| Age >65 yrs |
| Elevated systolic blood pressure |
| Elevated pulse pressure |
| Obesity |
| Hypertension |
| Coronary artery disease |
| Diabetes mellitus |
| Atrial fibrillation |
| Echocardiography |
| Left atrial enlargement |
| Concentric remodeling (relative wall thickness >0.45) |
| Left ventricular hypertrophy |
| Elevated left ventricular filling pressures (grade II to IV diastolic dysfunction) |
| Interim evaluation (after echocardiography) |
| Symptomatic response to diuretic drugs |
| Exaggerated increase in systolic blood pressure with exercise |
| Re-review of chest radiograph consistent with heart failure |

Hoeper et al. JACC 2009;54:S85-96

# 6 MINUTE WALK

- Distance ambulated in 6 minutes
- Can be performed on or off oxygen
- Surrogate outcome measure in most PH trials of pharmacologic therapy
- Emphasizes that PH therapy is primarily focused on improving symptoms
  - Mortality benefit has not been proven

# MECHANISM OF TREATMENT




Humbert M et al. NEJM 2004;351:1425-36

# PH TREATMENT

- Endothelin receptor antagonist (ERA)
  - Bosentan (Tracleer)
  - Ambrisentan (Letairis)
- PDE inhibitors
  - Sildenafil (Revatio)
  - Tadalafil
- Prostacyclin derivatives
  - Flolan (IV)
  - Remodulin (IV / SQ)
  - Iloprost (inhaled)

# HAS PH THERAPY BEEN SHOWN TO WORK?

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YES!

NO

NO

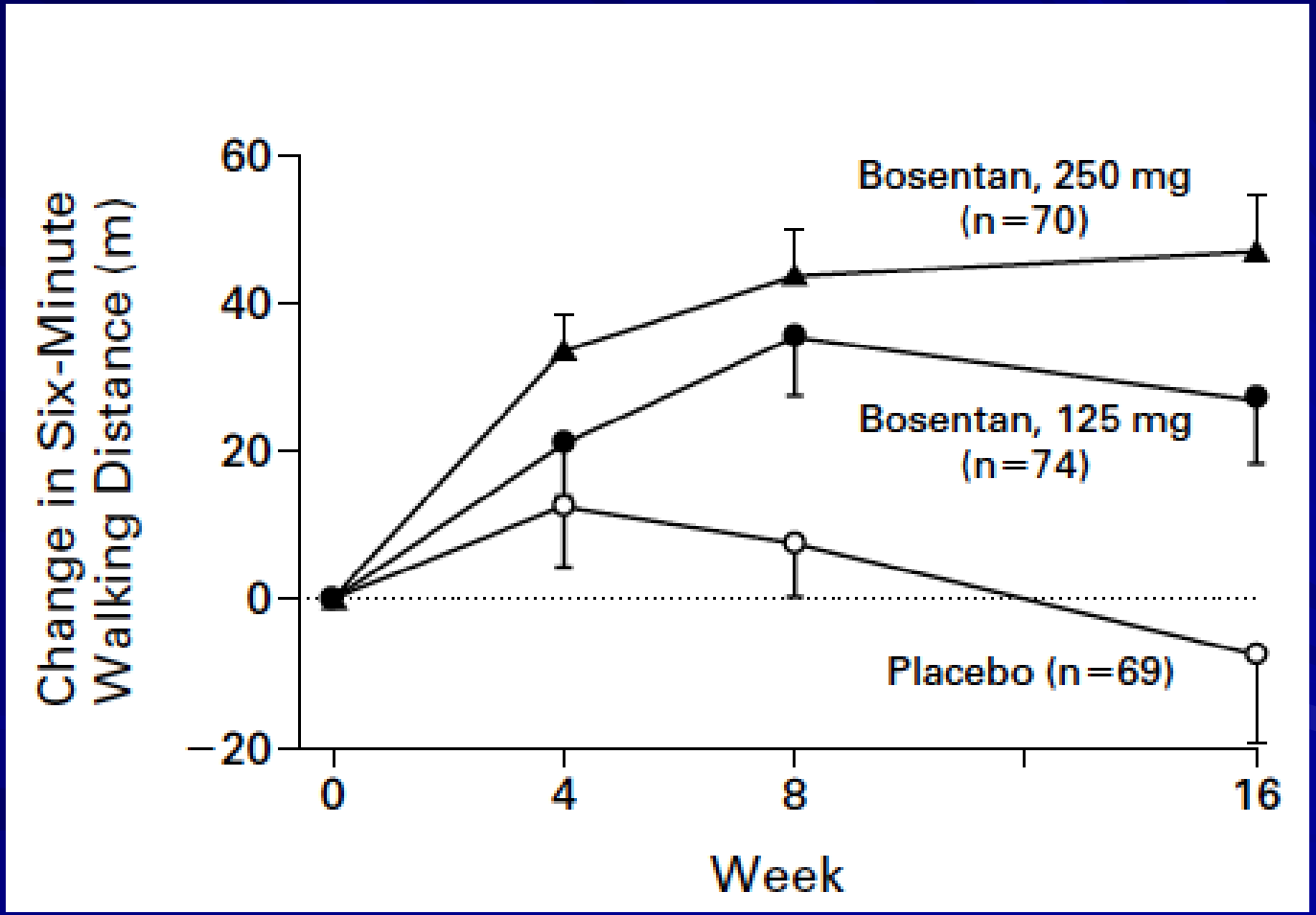
NO, BUT SURGERY DOES

Simonneau et al. JACC 2009;54: S43-54

# BOSENTAN

- Dual endothelin-receptor antagonist
- First orally available therapy for PAH
- Marketed as Tracleer
- High incidence of hepatoxicity
  - LFTs checked qmonthly
  - 10% will show elevated LFTs with treatment

# BREATHE TRIAL
# BOSENTAN



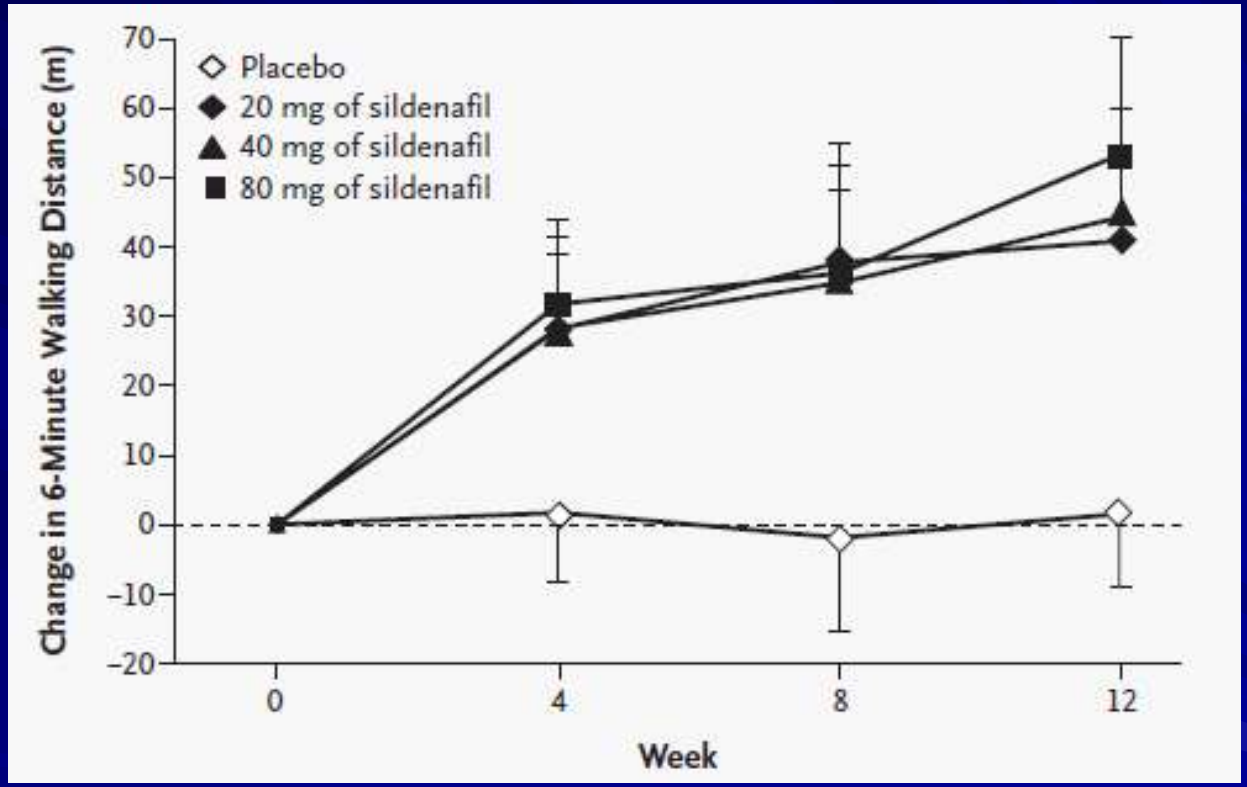

Rubin et al. NEJM 2002;346:896-903

# SUPER TRIAL
# SILDENAFIL

- 278 patients with symptomatic PAH were randomized to 12 weeks of sildenafil (Revatio) versus placebo
  - RHC required with mean PAP > 25 mm Hg and PCWP < 15 mm Hg
  - Primary endpoint: 6 minute walk distance

- 3 doses of Revatio:
  - 20 mg tid
  - 40 mg tid
  - 60 mg tid

# SUPER TRIAL




Galie et al. NEJM 2005;353:2148-57

# SUPER TRIAL

- Sildenafil improves exercise capacity and functional class in PAH patients
- Side effects include flushing and diarrhea
- Quite expensive!
  - May be better once sildenafil is generic although same dose cannot be used
  - Medication needs to be approved by insurance before starting treatment
- No *strong* evidence for benefit in patients with lung disease, elevated PCPW, LV dysfunction, or chronic PE
  - But it is still used in these patients!
  - Small studies have suggested benefit in those with LV dysfunction and secondary PH

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# ANTICOAGULATION

- PH patients are at increased risk for intrapulmonary thrombosis and thromboembolism
- Anticoagulation with Coumadin (target INR 2.0) is recommended in patients with PAH, group 1
- No randomized controlled evidence
- Evidence based on retrospective studies

# CONCLUSIONS

- Echocardiography can suggest PH, but right heart catheterization is needed to confirm the diagnosis
- Determination of etiology is important as it impacts upon treatment, but can be difficult in clinical practice
- Medical therapy best studied in Group1 PAH patients

Navin Rajagopalan, MD

University of Kentucky

859-317-0775 (cell)

nra224@uky.edu

Transplant referral: 1-800-456-5287