Caring for the patient with pulmonary hypertension

Lindsay Castle, DO FACC
Heart Disease Management Clinic
OhioHealth Riverside Methodist Hospital

Overview

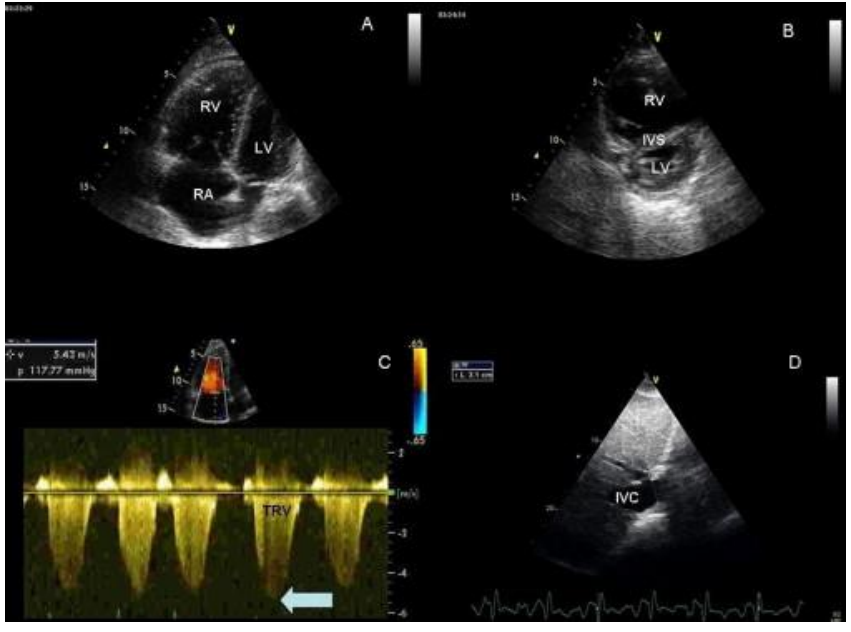
- Definition of pulmonary hypertension
- Presentation
- Diagnostic evaluation
- Treatment
- Safety of exercise in PH patients
- PH patient care at OhioHealth RMH

Definition

- **mean pulmonary artery pressure (mPAP) > 20 mmHg**
  - PVR > 2 Wood units → pre-capillary pulmonary hypertension
    - relatively low wedge pressure and high mean PA pressure
    - RV enlargement with reduced RV function
    - one type of pre-capillary pulmonary hypertension (PH) is pulmonary arterial hypertension (PAH)
  - PVR < 2 Wood units → post-capillary pulmonary hypertension
    - relatively high wedge pressure from left heart disease and lower mean PA pressures
    - less RV enlargement and dysfunction
  - can have combined pre-capillary/post-capillary pulmonary hypertension
    - relatively high wedge pressure from long term left heart disease but also very high PA pressures
    - RV enlargement with reduced RV function

Presentation

- dyspnea
- edema
- lightheadedness and/or syncope
- abnormal echocardiogram
  - RV enlargement with reduced RV function
  - elevated estimated RVSP
  - PH is likely if RVSP is greater than 50mmHg
  - significant PH is unlikely if RVSP is < 35mmHg
- history of pulmonary embolism
- scleroderma or other autoimmune disease
- family history of pulmonary hypertension



www.onlinejase.com/article/S0894-7317(12)00800-0/fulltext

Causes

- familial
- idiopathic
- autoimmune disease
- drug/toxin
- HIV
- portal hypertension
- congenital heart disease
- left sided heart disease
- COPD
- ILD
- OSA
- CTEPH
- sarcoidosis
- sickle cell anemia
- splenectomy
- metabolic diseases

Evaluation

- echocardiogram
  - RVSP estimate
  - RV size and function
  - evidence of left heart disease and/or valvular heart disease
- right heart catheterization/LVEDP/shunt run
- cardiac MRI
- PFTs
- sleep study
- CT chest without contrast
- V/Q scan
- 6 minute walk test

- labs
  - CMP
  - CBC
  - NTproBNP
  - HIV
  - hepatitis screening panel
  - sedimentation rate
  - anticentromere antibody
  - ANA
  - RF
  - TSH
- history of drug use
- history of weight loss medication use
- family history of pulmonary hypertension

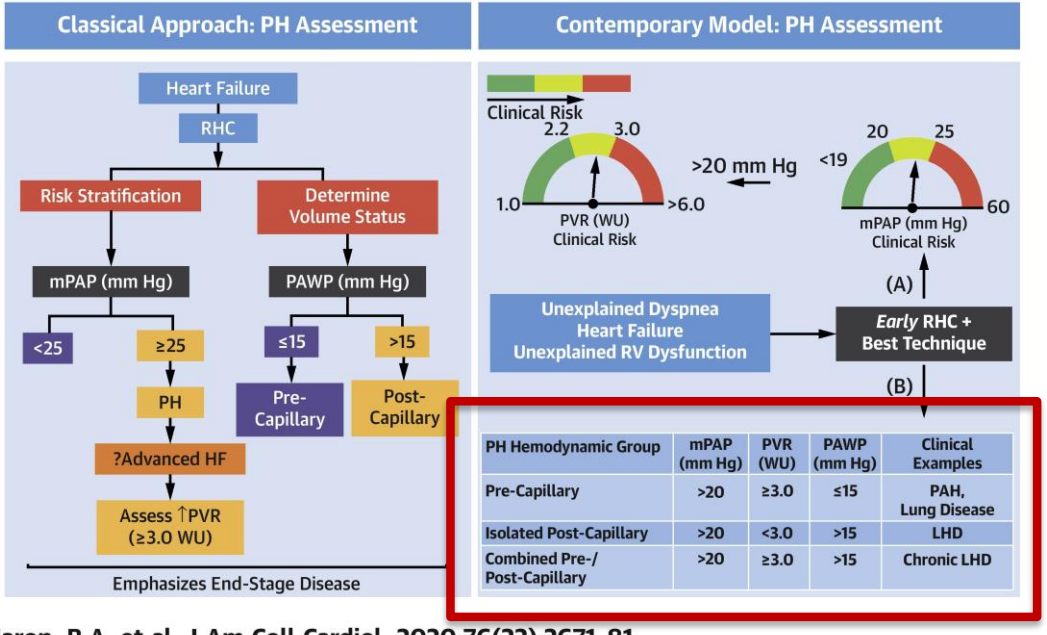
PVR = 80 x (mPAP – PAOP) / CO

Classification of PH

- mPAP
- PAWP
- PVR

Other diagnostic testing

CENTRAL ILLUSTRATION: A Comparison Between Classical and Contemporary Models for Interpreting Hemodynamic Results From Right Heart Catheterization to Classify and Risk Stratify Patients With Pulmonary Hypertension



PH Hemodynamic Group	mPAP (mm Hg)	PVR (WU)	PAWP (mm Hg)	Clinical Examples
Pre-Capillary	>20	≥3.0	≤15	PAH, Lung Disease
Isolated Post-Capillary	>20	<3.0	>15	LHD
Combined Pre-/ Post-Capillary	>20	≥3.0	>15	Chronic LHD

Maron, B.A. et al. J Am Coll Cardiol. 2020;76(22):2671-81.

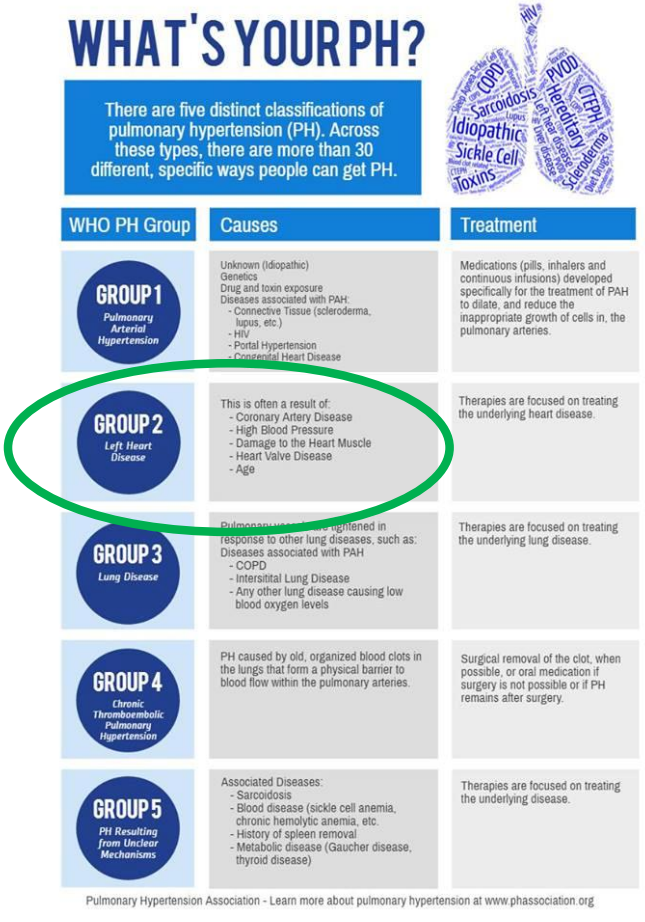
Pulmonary Hypertension Classification

Classification of PH

- mPAP
- PAWP
- PVR
- PAH reserved for WHO group I

Other diagnostic testing

This isn't always as easy as it appears…



WHO Group I PAH treatment

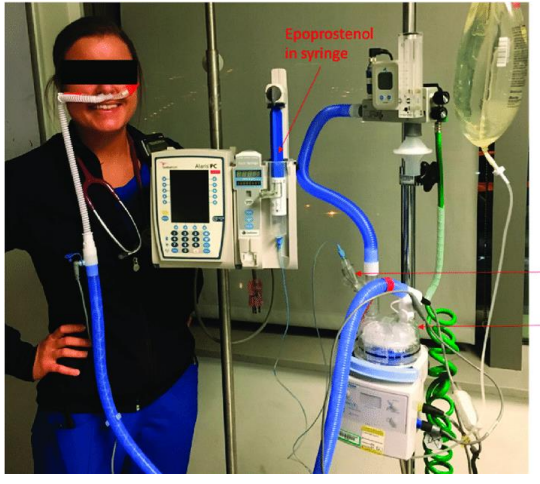
- **Endothelin receptor antagonists (ERA)**
  - *bosentan*, macitentan, ambrisentan
  - Category X
- **Phosphodiesterase type 5 inhibitor (PDE-5)**
  - sildenafil, tadalafil
- **Prostacyclin derivatives**
  - epoprostenol, treprostinil
  - inhaled, IV, SQ, oral formulations
- **Prostacyclin receptor agonists**
  - selexipag
- **Soluble guanylate cyclase stimulator**
  - riociguat
  - Category X

- side effects
  - flushing
  - headache
  - nasal congestion
  - peripheral edema
  - GERD/dyspepsia
  - N/V/D
- drug-drug interactions
  - PDE-5 inhibitors and nitrates
  - PDE-5 inhibitors and riociguat
  - risk for life threatening hypotension
  - add nitrates to “allergy” list

WHO Group I PAH treatment

www.tyvaso.com

www.veletri.com



www.emcrit.org

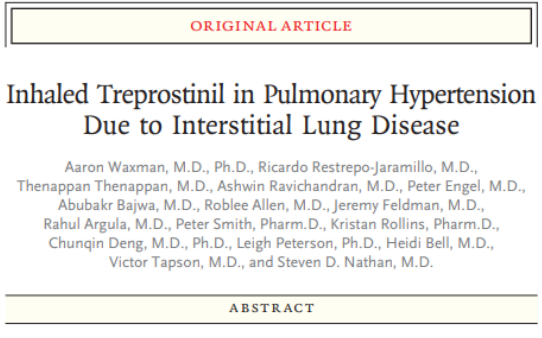
WHO Group II PH Treatment

- Treat the underlying disease process…
  - afterload reduction
  - loop diuretics to maintain euvolemia
  - blood pressure control
  - revascularization for CAD
  - amyloid disease modifying agents
  - valve repair or replacement
    - tricuspid valve?
- In my clinical experience…
  - spironolactone
  - digoxin
- Morbidity and mortality is high especially in patients with RV dysfunction.

Ghio S et al. J Am Coll Cardiol 2001; 37: 183.
Hemnes AR et al. Circ Res 2017; 121: 1136.
Miller WL et al. Circ Cardiovasc Imaging 2014; 7: 330.

WHO Group III PH

- Pulmonary hypertension secondary to lung disease
  - COPD
  - interstitial lung disease
  - chronic hypoxemia secondary to obesity hypoventilation syndrome
  - *sleep apnea*
- Treat the underlying disease process…
  - oxygen to maintain saturations > 90%
  - treatment of nocturnal hypoxemia
  - treatment of underlying lung disease
  - smoking cessation



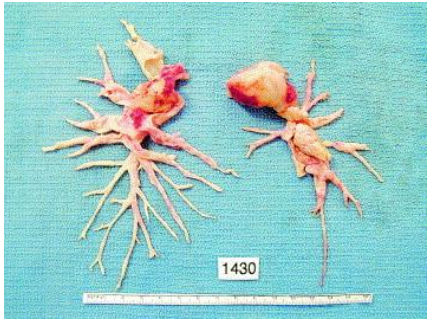
ORIGINAL ARTICLE

Inhaled Treprostinil in Pulmonary Hypertension Due to Interstitial Lung Disease

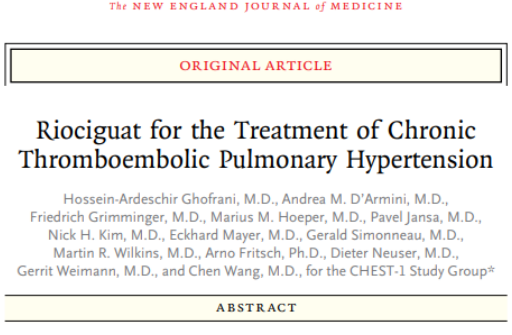
Aaron Waxman, M.D., Ph.D., Ricardo Restrepo-Jaramillo, M.D., Thenappan Thenappan, M.D., Ashwin Ravichandran, M.D., Peter Engel, M.D., Abubakr Bajwa, M.D., Roblee Allen, M.D., Jeremy Feldman, M.D., Rahul Argula, M.D., Peter Smith, Pharm.D., Kristan Rollins, Pharm.D., Chunqin Deng, M.D., Ph.D., Leigh Peterson, Ph.D., Heidi Bell, M.D., Victor Tapson, M.D., and Steven D. Nathan, M.D.

ABSTRACT

WHO Group IV PH Treatment



- abnormal V/Q scan
- anticoagulation indefinitely
  - warfarin
  - direct oral anticoagulant (DOAC)?
- referral to CTEPH center of excellence
  - pulmonary hypertension specialists, intensivists, radiologists, cardiothoracic surgeons, cardiac anesthesiology
- Pulmonary endarterectomy is treatment of choice
  - proximal clot amenable to surgical removal
  - resection of thrombi will lower PVR
  - no limiting comorbid conditions


The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Riociguat for the Treatment of Chronic Thromboembolic Pulmonary Hypertension

Hossein-Ardeschir Ghofrani, M.D., Andrea M. D'Armini, M.D., Friedrich Grimminger, M.D., Marius M. Hoeper, M.D., Pavel Jansa, M.D., Nick H. Kim, M.D., Eckhard Mayer, M.D., Gerald Simonneau, M.D., Martin R. Wilkins, M.D., Arno Fritsch, Ph.D., Dieter Neuser, M.D., Gerrit Weimann, M.D., and Chen Wang, M.D., for the CHEST-1 Study Group*

ABSTRACT

Jamieson SW et al. Annals Thor Surg 2003; 76:1457-64.

WHO Group V PH

- sarcoidosis
- blood disorders
  - sickle cell anemia
  - chronic hemolytic anemia
- inborn errors of metabolism
- thyroid disease
- ESRD

- Treat the underlying disease process…
- Limited evidence for use of pulmonary vasodilators

Is it safe to let patients with pulmonary hypertension exercise?

Things to consider…

- different types of pulmonary hypertension
- different degrees of left and right heart failure
  - evidence for benefit of cardiac rehab in patients with heart failure
- inpatient versus outpatient therapy
- Little evidence in the medical literature for exercise or rehab in patients with pulmonary hypertension.
  - Historically, it was thought that exercise could be dangerous.
- Patient may require supplemental oxygen.
- Patient may be anticoagulated.

Safety of exercise in PH patients

- Patients can have symptoms including exertional dyspnea, presyncope and even syncope.
- PH patients instructed to avoid exertion due to concerns for increased risk of worsening RV failure and/or sudden cardiac death.
- Patient with higher physical activity level have better long term survival.
- Studies provide evidence that exercise is safe and can be beneficial.
  - Respiration in 2011
  - European Respiratory Journal in 2012
    - stable condition
    - on pulmonary vasodilator therapy
    - under close supervision of provider at PAH center
    - training specially designed for PH patients

Established in 1871

Swiss Medical Weekly

Formerly: Schweizerische Medizinische Wochenschrift

An open access, online journal • www.smw.ch

Review article: Medical guidelines | Published 07 July 2017 | doi:10.4414/smw.2017.14462
Cite this as: Swiss Med Wkly. 2017;147:w14462

Rehabilitation in patients with pulmonary arterial hypertension

Keusch Stephan[a], Turk Alexander[a], Saxer Stéphanie[b], Ehlken Nicola[c], Grunig Ekkehard[c], Ulrich Silvia[b], on behalf of the Swiss Society of Pulmonary Hypertension

[a] Department of Pulmonology, Zürcher RehaZentrum Wald, Switzerland
[b] Pulmonary Clinic, University Hospital Zurich, Switzerland
[c] Thorax Clinic, University of Heidelberg, Germany

Figure 1: Effects of exercise training in PAH patients. Adapted from [26].

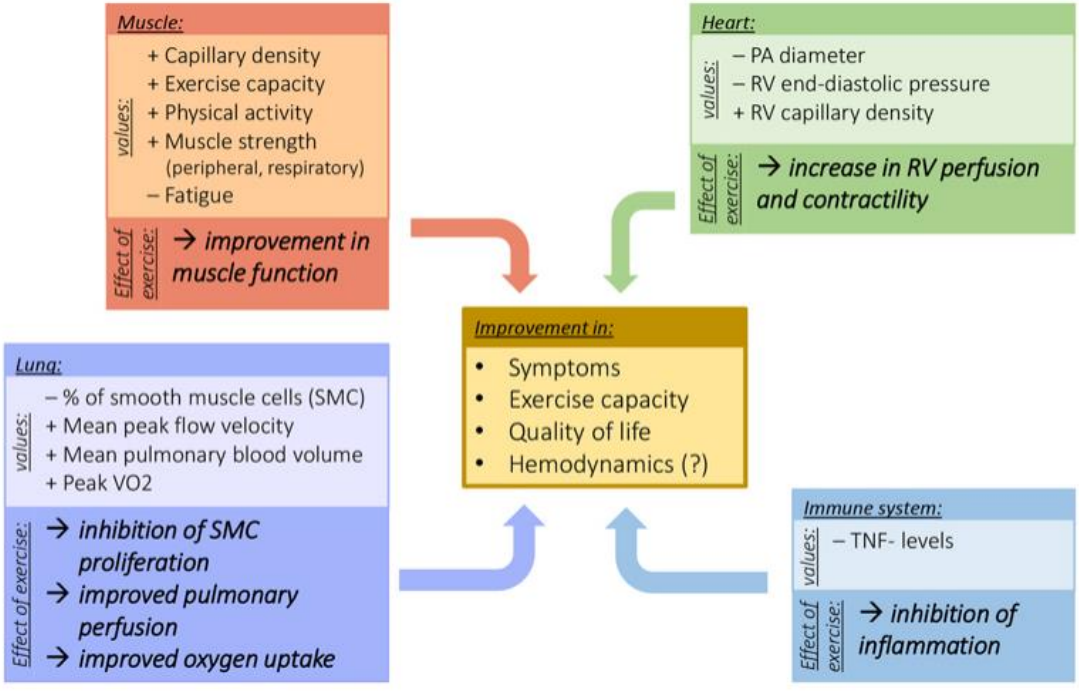


Table 1: Different components of the rehabilitation programme in patients with pulmonary arterial hypertension (PAH).

Intervention	Comment
Expert education and supervision	It is a prerequisite for training in PAH to perform this in collaboration with a PAH expert centre with programmes specifically tailored to groups of PAH patients.
Aerobic exercise training	Low workload, e.g., aerobic bicycle training (40–80% of peak exercise capacity). Monitoring oxygen saturation (>90%) and heart rate (<120/min). For 10 to 25 minutes. Frequency: daily.
Resistance training	Dumbbell with low weights for 30 minutes. Frequency: 5 times/week.
Mental walking training	Guidance in exploring individual physical limits and pacing. Frequency: several times/week.
Respiratory therapy	For 30 minutes. Frequency: 5 times/week.
Psychological support	If needed.
Nutritional support	If needed.
Social service	If needed.
Instruction in inhalation device	If needed.

No worldwide consensus:

- 3 weeks inpatient training
- home based training

Improvement in 6MWT distance has been replicated in many studies.

Self reported compliance rates were high. Effects are sustainable with improved long-term survival.

Table 2: Safety precautions and adverse effects of exercise training in pulmonary arterial hypertension (PAH).

Safety precautions
Inclusion of stable patients on optimised PAH targeted therapy and without signs of heart congestion after a thorough assessment in an expert centre
Intensively supervised start of the exercise programme, if possible in an in-hospital setting
Continuously supervised exercise training by experts
Avoidance of exhausting exercise (low workload ; training range between 40 and 80% of peak exercise capacity)
Adequate oxygen supplementation; avoidance of deep desaturation
Dumbbell training of single muscle groups with low weights
Potential adverse effects to be considered and immediately treated
Respiratory infections
Presyncope, syncope, dizziness, hypotension
Arrhythmias
Haemoptysis

Most common adverse event was respiratory infection requiring temporary discontinuation of training.

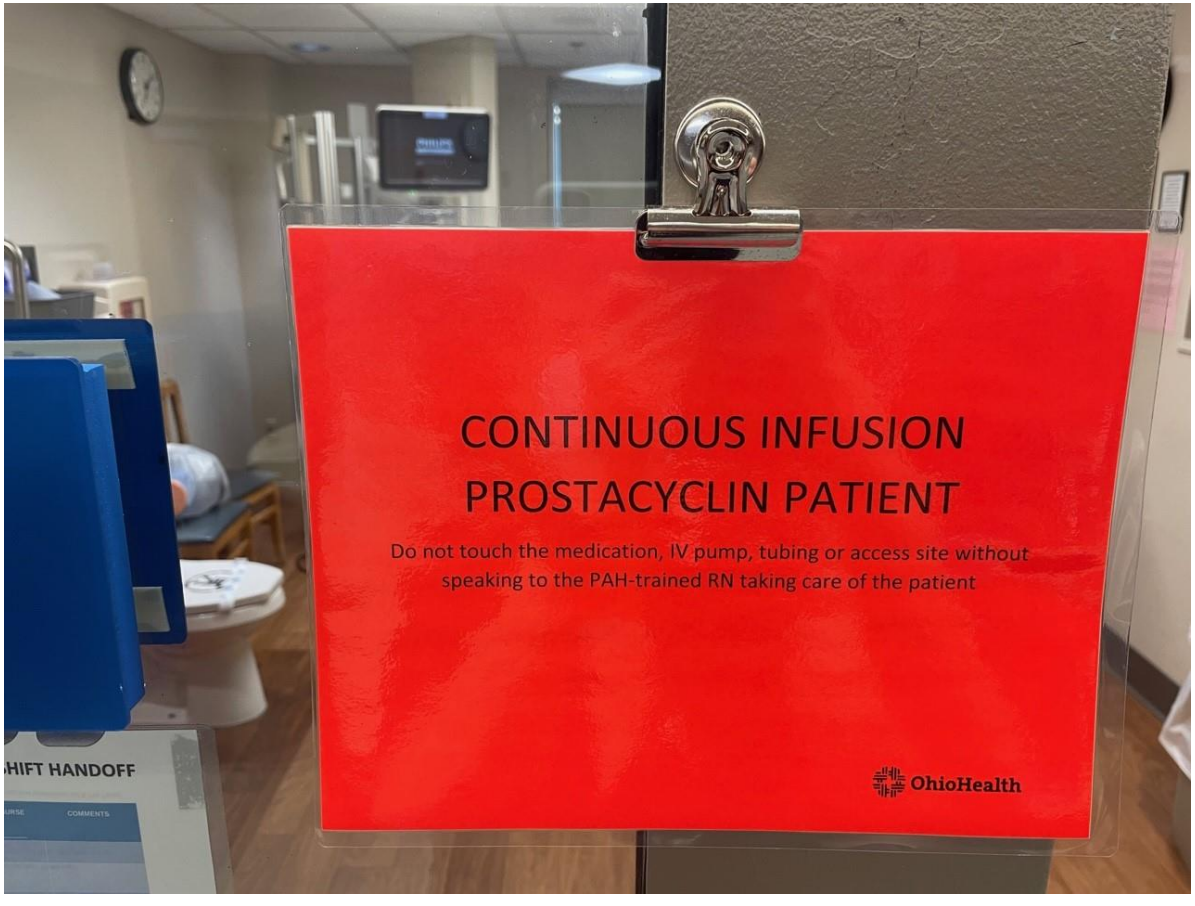
PAH patients are often unaware of their own limitations.

PH patient care at OhioHealth RMH

- We are seeing patients with all types of pulmonary hypertension in the HDMC and the pulmonology practice in Dublin.
- We have about 100 patients on pulmonary vasodilators.
- We can…
  - administer inhaled epoprostenol in ICU
    - patient in shock from right heart failure
  - we can start IV or SQ prostacyclin therapy for PAH
  - we can hospitalize patients on IV or SQ prostacyclin therapy at home
  - administer oral pulmonary vasodilators for inpatients

Signage for patient on IV or SQ continuous prostacyclin infusion

Stickers on IV tubing



Summary

- PH is a common condition that can result in significant patient debility.
- Must determine etiology of PH to treat it correctly!
- Safety first…
  - PH patient must be clinically stable.
  - Exercise should begin in “inpatient” setting.
  - Start at a very low workload
  - Oxygen saturation > 85%
  - Heart rate < 120 but take resting heart rate into consideration
  - Teach patient to accept the disease and understand their limitations.
  - Never hesitate to reach out to PH provider for guidance.

Questions?

References

2022 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension. Eur Respir J 2022 Aug 30;2200879. Online ahead of print.

Diagnosis and treatment of pulmonary arterial hypertension: a review. JAMA. 2022 Apr 12;327(14):1379-1391

Pulmonary hypertension: Abrief guide for clinicians. Mayo Clin Proc. 2020 Sep;95(9):1978-1988.

Management of pulmonary arterial hypertension. J Am Coll Cardiol. 2015 May 12;65(18):1976-97.

Rehabilitation in patients with pulmonary arterial hypertension. Swiss Med Wkly. 2017 Jul 7;147w14462.