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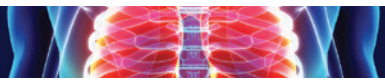
FALL 2019

THE DIVISION OF PULMONARY, ALLERGY AND CRITICAL CARE MEDICINE AT UPMC



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The UPMC Comprehensive Pulmonary Hypertension Program

Since 2009, the UPMC Comprehensive Pulmonary Hypertension Program has been diagnosing, treating, and following patients with pulmonary hypertension (PH). Utilizing a multidisciplinary approach that combines the expertise of cardiologists, pulmonologists, sleep specialists, and transplant and cardiothoracic surgeons in the evaluation and treatment of pulmonary vascular disease, our program is well-suited to manage complex patient cases that present diverse etiologies and pulmonary hypertension.

We offer our patients effective and efficient care through:

Early referral: Patients who are evaluated and treated for PH early in the disease process have improved outcomes. Ideally, we should see patients in the early stages of their diagnosis, and even before a formal diagnosis has been made, when there is suspicion by clinical symptoms or echocardiogram. We also see patients with a long-standing diagnosis who are already on therapy, but whose physicians are seeking another opinion, or are interested in advanced intravenous therapy or evaluation for surgery or transplantation.

Rapid diagnostic evaluation: Our goal is to provide the highest level of comprehensive and expedited care. We strive to complete all testing within weeks of the initial visit. For non-local or more symptomatic patients, we can often accommodate a clinic visit to conduct any remaining tests or right heart catheterization within a two-day period.

Initiating or modifying therapy: Our clinic has cultivated a close relationship between patient care and clinical/translational research. UPMC is currently involved in more than nine clinical studies (see page 5), and therefore can offer many patients novel therapies. In addition to enrollment in clinical trials, our nurses, nurse practitioners, social workers, and case managers help navigate the path to implementation of FDA-approved therapies.

Pulmonary Hypertension Group: Types of Conditions We Help Manage

Group I	Idiopathic pulmonary arterial hypertension (PAH) Drug-induced PAH PAH associated with connective tissue disease HIV-associated PAH Congenital heart disease
Group II	Diastolic dysfunction Systolic dysfunction Valvular heart disease
Group III	Parenchymal lung diseases due to emphysema or interstitial lung disease Sleep disordered breathing
Group IV	Chronic thromboembolic disease
Group V	Pulmonary hypertension associated with other diagnoses (e.g., sarcoidosis, sickle cell disease)

Follow-up care: Our policy is to follow up with each patient after their initial visit to our clinic. In addition, should we identify other conditions related to the patient's PH, such as connective tissue disease, liver disease, or other conditions, we can easily refer them for their respective clinical evaluation, as we work closely with physicians in the many divisions throughout UPMC.

Referrals: We recognize that patients may already have a pulmonologist or cardiologist involved in their care. Our goal is to work with the patient's existing team in the co-management of the patient. All referred patients will return to the referral center for continued follow-up. We look forward to working with clinicians in helping serve the needs of patients with PH. To make referrals, please call 1-877-PH4-UPMC or email PHprogram@upmc.edu.

The Advanced Cardiopulmonary Exercise Testing (ACPET) Program at UPMC

by Michael G. Risbano, MD, MA, FCCP

The initial evaluation for patients referred with breathlessness or fatigue with exertion often utilizes resting diagnostic studies including echocardiography, pulmonary function tests, chest imaging, and blood work. While these tests may assist in diagnosing disease states, physiologic abnormalities and the prominence of a disease state in patients with multiple cardiopulmonary disorders often cannot be determined. Provocative testing with advanced cardiopulmonary exercise testing (ACPET) challenges the cardio-pulmonary-vascular and skeletal muscle systems to elicit a cascade of physiologic events not measurable at rest.[1,2] The ACPET Program was instituted at UPMC Presbyterian Shadyside in June 2017, and since then, over 120 cases have been performed on patients with various cardiopulmonary disorders.

What Is ACPET?

Advanced cardiopulmonary exercise testing includes breath-by-breath analysis of ventilatory gas exchange and invasive measurement of pulmonary vascular and cardiac function in association with upright cycle ergometer and electrocardiogram (ECG) exercise testing.[3] ACPET provides full physiologic assessment of patients referred for exertional dyspnea and fatigue. With the ACPET modality, cardiac output, pulmonary artery pressures, multiple ventilatory indices, systemic pressures, and ECG variables are simultaneously assessed during a progressive intensity exercise provocation. Performing the study in the upright, seated position on a stationary bicycle ergometer replicates daily activities as almost all efforts are performed against gravity in the upright position (see Figure 1).

ACPET can delineate disease states related to pulmonary arterial, pulmonary venous, cardiac valvular, loading dynamics, autonomic, and skeletal muscle pathophysiologies that limit exercise capacity. Non-invasive CPET testing can be safely performed in patients with various disease states such as pulmonary arterial hypertension;[4] however, without the invasive component, the pulmonary vascular pressures and resistances, as well as cardiac output, are unknown. With ACPET, there is direct measurement of cardiopulmonary vascular hemodynamics, which provides gold standard information about hemodynamic response to exercise in conjunction with ventilatory mechanics and breath-by-breath analysis.

How Is the ACPET Performed?

ACPET at UPMC Presbyterian Shadyside involves the placement of a pulmonary artery catheter into the right internal jugular vein (see Figure 2) and a radial arterial line under ultrasound guidance in the cardiac catheterization lab. A resting supine pulmonary artery (PA) catheterization is performed to establish baseline values. The resting portion may include a shunt run or response to pulmonary vasodilators, if indicated. Once completed, the patient is seated in an upright position and cardiopulmonary hemodynamics are re-measured, as a change in body position often affects pressures, vascular resistance, and cardiac outputs. The patient is then connected to the CPET/metabolic cart, to obtain baseline resting values. Pulmonary gas exchange is measured with the Ultima™ CardiO_2 gas exchange analysis system by Medical Graphics Corporation (St. Paul, Minn.).

Shortly after, the patient is placed on the stationary bicycle in the cardiac cath lab where the stages of freewheel (no resistance applied) and four to five stages of ramped exercise are performed. The ramp chosen depends upon the patient's demographics and level of personal fitness. Hemodynamics and blood work are obtained every two minutes during exercise. Simultaneous blood gas measurements taken from the pulmonary artery and radial artery catheter allow for measurement of direct Fick cardiac output as well as oxygen saturations and lactate levels. We routinely calculate oxygen content from the pulmonary artery and radial artery to assess for peripheral oxygen extraction. Patients exercise until limited by symptoms of fatigue, leg fatigue, dyspnea, chest pain,

Figure 1: ACPET in action in the Cardiac Cath Lab at UPMC Presbyterian.

or a combination of these symptoms. If a patient is not limited by symptoms, the study is completed after eight to 12 minutes of exercise, preferably a peak exercise study. Finally, a cool down is done and recovery hemodynamics are measured.

Pulmonary arterial hypertension is defined as a resting mean PA pressure (mPAP) >25 mmHg and pulmonary vascular resistance (PVR) >3.0 Wood units (WU). Normal resting hemodynamics are mPAP <25 mmHg and PVR <3.0 WU. We define exercise pulmonary arterial hypertension while upright as mPAPpeak >30 mmHg, total pulmonary resistance (TPRpeak) >3.0 WU with a pulmonary arterial wedge pressure (PAWP) peak <20 mmHg. If the PAWPpeak is >20 mmHg, this constitutes an abnormal pulmonary venous response to exercise and may indicate heart failure with preserved ejection fraction (EF) in patients with a normal EF percentage and no valvular disease.

Indications for ACPET Referrals and Patient Populations of Interest

Patients referred for ACPET will include those with complaints of dyspnea on exertion or exercise fatigue that has not been fully explained by previous studies, or the causative disease state is unclear. The majority of patients referred to the ACPET Program will have been seen by either a primary care physician or a subspecialty physician, such as a pulmonologist, cardiologist, rheumatologist, or geriatrician.

Patients referred for testing may include those with dyspnea and histories of connective tissue disease (scleroderma in particular), diastolic dysfunction (heart failure with preserved ejection fraction), pre-pulmonary or pre-cardiac transplant, valvular heart disease, post-pulmonary embolism, parenchymal lung disease (interstitial lung disease, chronic obstructive pulmonary disease, cystic fibrosis), peripheral myopathy, and various forms of pulmonary hypertension, including pulmonary arterial hypertension.

Initial routine testing is required prior to performing ACPET including echocardiogram, pulmonary function testing, and chest imaging. As previously mentioned, for some patients these tests may be unrevealing or may demonstrate

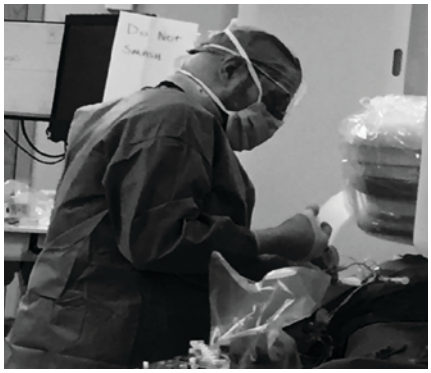

Figure 2: Dr. Michael Risbano performing a right heart catheterization.

multiple abnormalities such as concomitant lung disease and pulmonary hypertension or diastolic dysfunction. This technique provides a comprehensive ACPET to study and diagnose all forms of abnormal cardiopulmonary vascular and musculoskeletal responses to exercise for clinical and research purposes.

Impact of the ACPET Program

In a single-center study that performed a high volume of ACPETs, the authors demonstrated that the workup of exertional dyspnea in a multidisciplinary setting including ACPET dramatically reduced the time to diagnosis compared to routine testing alone.[5] Typical diagnoses made with the study include exercise pulmonary arterial hypertension, exercise pulmonary venous hypertension, ventilatory limitation, oxidative myopathy, and dysautonomia/preload insufficiency.[6]

Key benefits of ACPET include:

- Diagnosis of the etiology of exercise limitation or dyspnea on exertion not previously identified
- Development of a plan for intervention that may include pharmacologic, surgical, or cardiac/pulmonary rehabilitation therapies
- Identification of patients who may be eligible for clinical treatment trials or participation in investigational research trials

Our notable accomplishments include:

- Successful diagnosis of patients with exercise PAH with provocative exercise testing and treatment with pulmonary vasodilators, which resulted in reduced pulmonary vascular response to exercise and improved cardiac outputs with exercise.[7]
- Identification of an abnormal pulmonary vascular response to exercise in patients with chronic thromboembolic pulmonary disease, which led to successful treatment with balloon pulmonary angioplasty
- Diagnosis of a patient with cystic fibrosis using ACPET, which ultimately led to a successful lung transplant.

Commercial insurance typically covers the ACPET study.

Referral Information

For any patients who have continued dyspnea despite comprehensive testing and interventions, referrals can be made by calling 1-877-PH4-UPMC or emailing **PHprogram@upmc.edu**.

Referrals can also be made to Dr. Risbano directly at **risbanomg@upmc.edu**.

For more information about the ACPET Program, including patient information and frequently asked questions, please visit our website at **www.upmc.com/acpet**.

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Case Study: Advanced Cardiopulmonary Exercise Testing (ACPET) To Determine the Etiology of Multifactorial Dyspnea

by Quyen Nguyen, MD, and Michael G. Risbano, MD, MA, FCCP

Case Introduction

A 60-year-old WHO functional Class II female with a past medical history of hypothyroidism, sclerosis sine scleroderma (ANA 1:640 nucleolar, elevated aldolase levels and antibodies to Th/To), nonspecific interstitial pneumonia (NSIP), and pulmonary arterial hypertension, followed up at the UPMC Comprehensive Pulmonary Hypertension Clinic for ongoing dyspnea on exertion. She noted progressive dyspnea on exertion over the previous year, in particular on hills and stairs. She was treated with an upfront combination therapy of tadalafil and ambrisentan.[1,2]

In addition to pulmonary vasodilators, she was on aspirin and levothyroxine. She had no known history of venous thromboembolism, diet drug use, amphetamine or amphetamine derivative use, illicit drug use, HIV, miscarriage, or blood transfusion. Her social history was significant for never smoking, occasional alcohol use, and no significant occupational exposures in her work as an attorney.

Physical exam: BP 147/98, P 116, oxygen saturation of 96% on room air. She appeared younger than her stated age. No jugular venous distension. Chest exam with normal air movement, no crackles or wheezing. Cardiac exam with an enhanced second pulmonary closure was sound. No pedal edema. Her skin exam revealed dactylitis with chapped finger tips, without skin thickening, telangiectasias, or ulcerations.

Pulmonary function testing: FVC 1.78 liters (56% predicted), FEV1 1.42 liters (64% predicted), FEV1/FVC ratio 80%, TLC 4.90L (77% predicted), and DL_{CO} 22.91 (32% predicted).

Computed tomography angiography of the chest: Increase in subpleural interstitial markings and septal thickening consistent with nonspecific interstitial pneumonia (NSIP) pattern of interstitial lung disease (ILD) without honeycombing or fibrosis. There was no evidence of acute or chronic pulmonary embolus.

Echocardiogram: Normal left ventricular ejection fraction, mildly dilated right ventricle with TAPSE 1.8 cm, tricuspid regurgitation peak velocity of 3.3 m/s, and estimated pulmonary artery systolic pressure of 47 mmHg.

Ventilation/perfusion scan: Revealed no chronic thromboembolism.

Case Discussion and Initial Management

After one year on dual pulmonary vasodilator therapy, the patient had subjective improvement albeit persistent dyspnea on exertion, the etiology of which was unclear. She had mild radiographic progression of ILD, and echo showed decreased PASP to 22 mmHg.

Her six-minute walk distance was 365 m, where 300-400 m is considered intermediate risk for PAH.[3,4] She was referred for invasive cardiopulmonary resistance to quantify her respiratory and cardiovascular limitation and determine the role for augmentation of pulmonary vasodilator therapy versus possible immunosuppression for her ILD and scleroderma.

Advanced Cardiopulmonary Exercise Testing

Procedure description: The patient arrived at the cardiac catheterization lab at UPMC Presbyterian, was placed in the supine position, and was prepped and draped in a sterile fashion. A left radial arterial line and a right internal jugular 8F introducer was placed under ultrasound guidance. A Swan-Ganz VIP catheter was inserted. For the exercise portion, an ACPET was performed with the MGC Diagnostics metabolic cart. Continuous oxygen saturation, EKG, hemodynamics, and expired gas analysis were performed. Serial blood pressures were obtained from the arterial line. Resting seated and exercise measurements were obtained.

ACPET Discussion

The patient performed a maximal exercise study as indicated by an RER >1.1. She achieved a low VO_2 at anaerobic threshold and peak exercise indicating limitation of exercise capacity. There was little increase in VO_2 as the work rate increased. The patient had multiple abnormalities present in this study. She had resting pulmonary arterial hypertension. With exercise, her pulmonary artery pressures and total and pulmonary vascular resistance increased. However, this may not be limiting her exercise capacity as her cardiac output increased to 88% predicted peak cardiac output (based upon her VO_2 max achieved) at peak exercise. This indicates that it is unlikely that her pulmonary vascular disease was a limitation to exercise. Despite a maximal exercise result, the patient did not maximally extract oxygen at peak exercise as the pulmonary artery oxygen saturation was only 46%. At peak exercise this value can be as low as 25% in normal individuals. The lack of normal peripheral oxygen extraction at peak can be seen in patients with mitochondrial myopathies, which also results in a relatively elevated cardiac output at peak exercise despite low VO_2 max. Some of the CO that should be low because of pulmonary vascular disease may be offset by the presence of a concomitant metabolic myopathy. The primary exercise limitation is mostly due to ventilatory limitation. At peak exercise, the patient had an elevated breathing frequency, low breathing reserve, elevated VD/VT, high VE/VCO_2 at anaerobic threshold, and elevated A-a gradient.

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Table 1: Exercise parameters

Stage	RPE	VO_2 (mL/min)	RER	$P(A\text{-}a)O_2$	VD/VT
Rest Seated	6.0	231.0	0.8	17.4	0.41
Unloaded	7.0	436.0	1.1	44.2	0.32
1.0	9.0	481.0	1.0	36.7	0.34
2.0	9.0	594.0	1.1	43.0	0.33
3.0	11.0	712.0	1.2	49.0	0.32
Peak	15.0	880.0	1.4	61.2	0.37

RPE=rating of perceived exertion; RER=respiratory exchange ratio

Table 2: Exercise physiology at rest, anaerobic threshold, and peak exercise

	Exercise Time	Mets	Vt (L)	VE (L/min)	RR (br/min)	VE/MVV (%)	VO_2 Max (% predicted)	VE/VCO_2	$PETCO_2$
Rest		2.1	0.59	17.6	30	25		41	32
Anaerobic Threshold		2.6	0.87	27.2	61.8	39	38	40	31
Peak Exercise	9:33	3.7	1.04	61.8	59	89	56	50	25

Vt=tidal volume; **VE**=minute ventilation; **RR**=respiratory rate; **VE/MVV**=ratio of minute ventilation to maximal voluntary ventilation; **VE/VCO_2**=measure of ventilatory efficiency; **$PETCO_2$**=measure of pulmonary perfusion.

Table 3: Radial and pulmonary arterial blood gases

Stage	Arterial pH	Arterial $PaCO_2$ (mmHg)	Arterial PaO_2 (mmHg)	Arterial HCO_3- (mEq/L)	Base	Arterial SaO_2 (%)	Lactate	Arterial Hb	Venous pH	Venous $PaCO_2$ (mmHg)	Venous PaO_2 (mmHg)	Venous HCO_3- (mEq/L)	Venous SaO_2
Rest Seated	7.45	38.00	86.00	26.00	3.00	96.00	0.80	12.90	7.43	42.00	41.00	27.00	73.00
Unloaded	7.50	33.00	75.00	26.00	3.00	94.00	1.60	13.20	7.40	44.00	39.00	27.00	65.00
1.0	7.48	34.00	80.00	25.00	2.00	95.00	2.00	13.40	7.41	44.00	32.00	27.00	56.00
2.0	7.48	34.00	75.00	25.00	2.00	94.00	2.60	13.50	7.40	44.00	34.00	27.00	56.00
3.0	7.46	33.00	72.00	23.00	0.00	93.00	3.90	13.90	7.37	46.00	31.00	26.00	51.00
Peak	7.43	32.00	66.00	21.00	-2.00	0.92	6.40	14.10	7.34	51.00	30.00	27.00	46.00

Table 4: Invasive hemodynamics

Stage	Watts	HR (BPM)	SBP (mmHg)	DBP (mmHg)	MAP (mmHg)	RA (mmHg)	PAS (mmHg)	PAD (mmHg)	mPAP (mmHg)	PAWP (mmHg)	PA sat (%)	CO (L/min)	CI ($L/min/m_2$)	TPR (WU)	PVR (WU)	Stroke Volume (mL)
Rest Supine	0.0	73.0	126.0	50.0	75.3	5.0	45.0	19.0	30.0	11.0	67.0	6.3	3.7	4.8	3.0	85.8
Rest Seated	0.0	82.0	143.0	59.0	87.0	0.0	39.0	13.0	25.0	3.0	73.0	5.7	3.4	4.4	3.8	69.8
Unloaded	0.0	102.0	198.0	75.0	116.0	0.0	56.0	21.0	37.0	5.0	65.0	8.4	5.0	4.4	3.8	82.1
1.0	12.0	102.0	206.0	77.0	120.0	0.0	58.0	22.0	37.0	6.0	56.0	6.8	4.0	5.5	4.6	66.4
2.0	34.0	106.0	210.0	75.0	120.0	0.0	60.0	25.0	39.0	6.0	56.0	8.5	5.0	4.6	3.9	80.3
3.0	52.0	106.0	234.0	79.0	130.7	0.0	74.0	25.0	48.0	6.0	51.0	9.0	5.3	5.4	4.7	84.6
Peak	72.0	112.0	242.0	82.0	135.3	3.0	91.0	32.0	59.0	7.0	46.0	10.0	5.9	5.9	5.2	89.1

HR=heart rate; **SBP**=systolic blood pressure; **DBP**=diastolic blood pressure; **MAP**=mean arterial pressure; **RA**=right atrium; **PAS**=PA systolic; **PAD**=PA diastolic; **mPAP**=mean pulmonary artery pressure; **PAWP**=PA wedge pressure; **CO**=cardiac output; **CI**=cardiac index; **TPR**=total pulmonary resistance; **PVR**=pulmonary vascular resistance.

New Clinical Trials

The UPMC Comprehensive Pulmonary Hypertension Program is involved in many clinical trials with a focus on translating recent novel mechanistic drug discoveries to patients in phase I/II clinical trials across the spectrum of disease. For Group I pulmonary arterial hypertension (PAH), UPMC is the lead center of a phase I multicenter clinical trial of ABI-009, a novel formulation of the mTOR inhibitor sirolimus designed specifically for improved pulmonary vascular uptake to arrest vascular smooth muscle cell growth causing PAH. Additional Group I PAH studies include: the A DUE trial (Acetelion), a study of macitentan and tadalafil fixed dose combination therapy versus mono therapy; a two-week phase I(b) trial (Gossamer Bio) of an inhaled PDGFR inhibitor; and a 24-week phase II(a) study of Sotatercept (ACE-011) (Acceleron Pharmaceuticals) in functional Class 3 subjects that will evaluate treatment response with ACPET.

UPMC is one of only a few sites in phase II trials of recombinant human Angiotensin Converting Enzyme (rhACE2) and a sustained-released VIP analogue for PAH. UPMC participates in several national registries for PAH. For Group II pulmonary hypertension (PH), UPMC is running several NIH studies and participating in several industry-funded trials that could lead to the first approved therapy in pulmonary hypertension due to left heart disease, including studies of an oral formulation of nitrite, metformin specifically targeting Group II PH, the calcium sensitizer levosimendan, and macitentan. For Group III PH, UPMC is involved in several multicenter industry trials testing drugs approved for PAH in this patient population. UPMC is also involved in the Perfect trial (United Therapeutics), which will investigate the effect of inhaled treprostinil on PH related to COPD. Group IV trials include: A Study to Find Out if Selexipaq Is Effective and Safe in Patients with Chronic Thromboembolic; and Pulmonary Hypertension When the Disease Is Inoperable or Persistent/Recurrent After Surgery (SELECT).

For further information on PH clinical trials, contact Marc Simon, MD (**simoma@upmc.edu**) or Mary Kunkel, RN (**kunkelme@upmc.edu**), or call 412-647-4463.

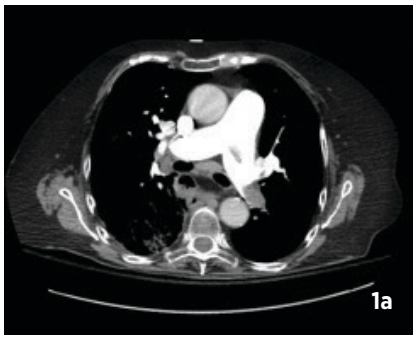
Pulmonary Embolism Response Team: A Multidisciplinary Approach to Treat a Complex Disease

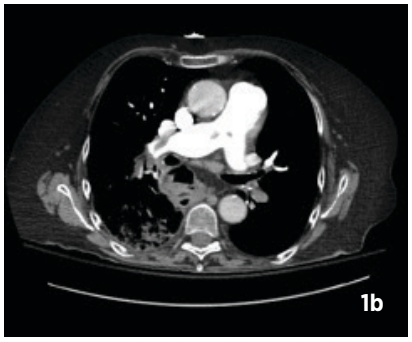
by Belinda Rivera-Lebron, MD, MS, FCCP

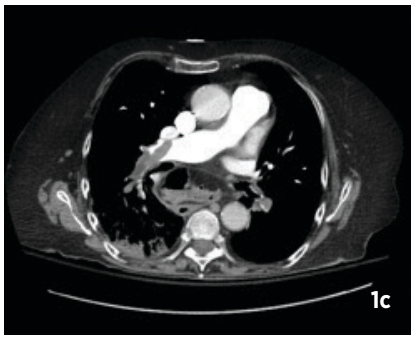
A 64-year-old female presents to the emergency department complaining of one week of cough and increasing dyspnea on exertion. Her symptoms had progressively worsened in 24 hours with associated scant hemoptysis and dull substernal chest pressure. She had a past medical history of a hypertension, hypothyroidism and deep vein thrombosis (DVT), and pulmonary embolism (PE) eight years ago, but had been off anticoagulation for the last six months. On presentation, her vital signs were: temperature 37°C, BP 109/56 mmHg, heart rate 108, respiratory rate 22, oxygen saturation of 92% on room air. Electrocardiogram (EKG) showed sinus tachycardia. Labs were remarkable for a troponin of 0.46 ng/mL (Normal < 0.1 ng/mL). A contrast-enhanced chest computed tomography angiography (CTA) was ordered (see Figure 1), which showed a saddle PE with extension into bilateral pulmonary arteries and an enlarged right ventricle (RV). She was started on a heparin infusion.

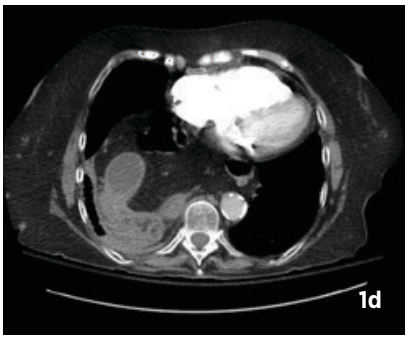
The Pulmonary Embolism Response Team (PERT) was consulted, and the patient was transferred into the intensive care unit (ICU) for closer observation.

On arrival to the ICU, the patient's vital signs were: temperature 36.1°C, BP 136/76 mmHg, heart rate 140, respiratory rate 34, oxygen saturation of 96% on 4 L nasal canula. On exam, she appeared in mild distress. She had clear lung sounds and no lower extremity edema. A transthoracic echocardiogram was done promptly on arrival (see Figure 2). It showed severe RV enlargement with hypokinesis, interventricular septal flattening, and McConnell's sign, which refers to a regional pattern of RV free wall dysfunction with sparing of the apex. A multidisciplinary PERT meeting took place between pulmonary and critical care medicine and interventional cardiology. The patient was risk stratified as intermediate-high risk PE with signs of hemodynamic decompensation, based on clinical appearance and increasing heart rate and oxygen saturation. A decision was made to perform catheter-directed thrombolysis, with an initial bolus of 1mg of tissue plasminogen activator (tPA) followed by an infusion at 1mg/hr for 12 hours. Heparin infusion was also continued with a low intensity protocol targeting anti-Xa range 0.2-0.5 units/mL. The next morning, her vitals were: temperature 36.5°C, BP 142/82 mmHg, heart rate 98, respiratory rate 18, oxygen saturation of 95% on 1 L nasal canula. Patient appeared more comfortable and reported feeling better. The catheters were removed, and she was transitioned to oral anticoagulation.

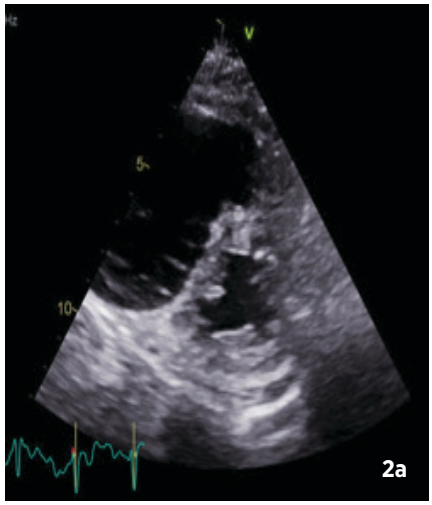


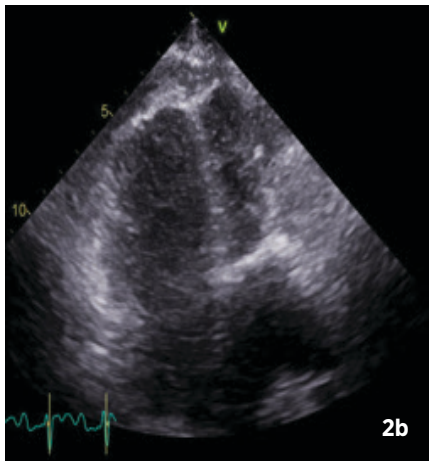






(Left) **Figure 1 (a-d):** Contrast-enhanced chest computed tomography angiography (CTA) showing saddle pulmonary embolism (Figure 1a-c), and enlarged right ventricle (Figure 1d).





(Above) **Figure 2 (a-b):** Transthoracic echocardiogram showing severe right ventricular enlargement and interventricular septal compression.

Pulmonary Thromboendarterectomy and Pulmonary Artery Balloon Angioplasty for CTEPH

by Belinda Rivera-Lebron, MD, MS, FCCP

Chronic thromboembolic pulmonary hypertension (CTEPH) is caused by mechanical obstruction from residual thrombi in the pulmonary arteries resulting in increased pulmonary vascular resistance (PVR), pulmonary hypertension (PH), and right ventricular failure.[1,2] Acute pulmonary embolism (PE) resolves in most cases. However, up to 4% of PE survivors develop CTEPH.[3-5] Most patients with CTEPH have experienced a PE in their lifetime; despite this, up to 25% of patients have never reported a thrombotic event.[6] In the U.S., approximately 600,000 people have an acute PE each year, of which up to 2,500 new cases are diagnosed with CTEPH each year.[7]

In addition to the transformation of incomplete resolution of thrombi into organized fibrotic scar tissue, CTEPH is a vascular disorder, with pulmonary arteriopathy in segments not affected by obstruction. The combination of thrombus obstruction and vascular remodeling results in PH, with increased right ventricle strain and eventual right-sided heart failure.

Patients may present with exertional dyspnea, fatigue, palpitations, lightheadedness, or syncope. CTEPH is diagnosed by precapillary pulmonary hypertension on right heart catheterization (mean pulmonary arterial pressure >25 mmHg and pulmonary arterial wedge pressure ≤15 mmHg) and abnormal ventilation perfusion scintigraphy (VQ scan) including at least one mismatched perfusion defect with confirmatory imaging by either computed tomography angiography (CTA) or pulmonary angiography after at least three months of effective anticoagulation.[2]

The Gold Standard: Pulmonary Thromboendarterectomy

Pulmonary thromboendarterectomy is the gold standard and only potentially curative therapy for CTEPH. Operability is determined by thrombus accessibility, hemodynamic severity, medical comorbidities, and expertise of the surgical team. However, not all patients are eligible for surgery. Furthermore, up to 35% of patients who undergo thromboendarterectomy may still have persistent PH after surgery.[5]

For inoperable patients and/or those with persistent pulmonary hypertension after thromboendarterectomy, medical therapy with riociguat, a soluble guanylate cyclase stimulator, has been shown to improve exercise capacity and pulmonary vascular resistance, and is the only FDA-approved drug for these patients.[8] In a long-term follow-up study, riociguat was shown to have sustained beneficial effects and was well tolerated.[9]

Balloon Pulmonary Artery Angioplasty as an Alternative Therapy

Balloon pulmonary artery angioplasty (BPA) is emerging as an alternative therapy for patients with inoperable or persistent PH after thromboendarterectomy. BPA, a catheter-based intervention to treat pulmonary artery obstruction, was initially described in CTEPH patients in 2001 with favorable hemodynamic effects results, but with increased complication rates, including reperfusion pulmonary edema.[10] With technique modifications, Japanese groups have dramatically improved outcomes by lowering the complication rate, while sustaining hemodynamic improvements. Serial BPA sessions have shown to improve mean pulmonary artery pressure, cardiac output, and functional class, and are a promising therapeutic strategy for the treatment of CTEPH.[11,12,13]

The UPMC CTEPH Program is a multidisciplinary team composed of pulmonary hypertension experts from pulmonary and critical care, cardiology, interventional cardiology, and cardiac surgery. Our team has the expertise in medical, surgical, and interventional treatments, including BPA, for CTEPH. Please refer your patients by calling 1-877-PH4-UPMC (744-8762).

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Introducing New Chief of the Division of PACCM: Alison Morris, MD, MS

After an extensive national search, **Alison Morris, MD, MS**, has been appointed chief of the Division of Pulmonary, Allergy and Critical Care Medicine (PACCM) as of July 1, 2019. She is the vice chair for Clinical Research in the Department of Medicine and has successfully led the Division of PACCM as interim chief since the fall of 2018. Dr. Morris is a professor of medicine with secondary appointments in Immunology and Clinical and Translational Research. She holds the UPMC Chair of Translational Pulmonary and Critical Care Medicine, and she is director of the University of Pittsburgh HIV Lung Research Center, as well as director of the Center for Medicine and the Microbiome.

To read the full announcement, please visit **UPMC.com/NewChiefPACCM**.

Division of Pulmonary, Allergy and Critical Care Medicine Upcoming Conferences

Pittsburgh Rust Belt Microbiome Conference
Nov. 4 – 5, 2019 — Pittsburgh, PA
https://events.mcs.cmu.edu/rbm2019
This conference will bring together the microbiome, microbial evolution, and pathogenesis research communities from academic institutions and medical centers in the Rust Belt region.

University of Barcelona and The University of Pittsburgh International Lung Conference
Nov. 11 – 12, 2019 — Barcelona, Spain
https://lungconf.pitt.edu
The focus of this conference will be translational research for precision respiratory medicine.

COPD 2020: Current Guidelines and New Directions
Dec. 7, 2019 — Pittsburgh, PA
http://dom.pitt.edu/paccm/conferences
This conference aims to change treatment approaches to COPD, based on an algorithmic evidence-based approach to clinical practice. Physicians and other health care workers will learn the benefits and risks of bronchoscopic lung volume reduction, as well as the benefits of non-invasive ventilation, and be better able to select patients who may benefit by referral for one of these procedures.

To learn more about how UPMC is transforming pulmonary, allergy and critical care medicine, go to **UPMCPhysicianResources.com/Pulmonology**.

UPMC PHYSICIAN RESOURCES

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About UPMC
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