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RESPIRATORY

Reader

Welcome to our 11th issue of the *Respiratory Reader*. In this issue, we highlight a topic of great interest among health care providers both inside and outside pulmonary medicine: pulmonary embolism (PE). Pulmonary embolism and deep vein thrombosis affect over 200,000 Americans each year, with a high rate of mortality as well as risk of long-term morbidity among survivors. The field has been rapidly evolving, from diagnosis and risk stratification, to management of acute PE with catheter-based technologies and surgical approaches. Additionally, there has been a renewed interest in diagnosis and management of chronic thromboembolic pulmonary hypertension (CTEPH), a life-threatening risk of unresolved PE that may affect 4 percent or more of PE survivors. We will share cases that highlight evolving clinical practices in the diagnosis and management of this disease. You will hear about our multidisciplinary initiatives in the management of Acute and Chronic PE: The Acute PE Team and CTEPH Program. These are UPMC initiatives focused on providing expedited state-of-the-art services to patients with life-threatening diseases, and we welcome opportunities to work with physicians in any way we can be of assistance in the management of acute and chronic PE.

We also welcome to our CTEPH team Thomas Gleason, MD. Dr. Gleason is well-known for his expertise in cardiothoracic surgery and serves as the director of the Center for Thoracic Aortic Disease. We look forward to having his surgical and pulmonary thromboendarterectomy experience in our growing CTEPH program.

(Continued on Page 2)

We welcome any suggestions or comments on how we might support you in the care of your patients. Please enjoy this issue of *Respiratory Reader*.

With great enthusiasm and respect,



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Team PHenomenal Hope — Racing to Make a Difference in 2015

After successfully completing the 2014 Race Across America, Team PHenomenal Hope (Team PH) is continuing its mission to raise awareness about pulmonary hypertension (PH) and funds to find a cure. Team PH is an amateur endurance sports team made up of individuals from the medical community and endurance community who share a passion for their sport and desire to race to make a difference. This year, we recruited several team members who are UPMC employees, drawing from our strong and talented base of athletes right here at home, as well as bringing in talent and passion from the race community in Ohio. Made up of runners; cyclists; swimmers; and triathletes, in any month you'll find us training for, and competing in endurance and ultra-endurance races; from marathons (and further) to Ironman Triathlons, and ultracycling events.

Our goal is to put PH on the map, and with our 2015 schedule, you will see our jerseys in races all over the country, and world. Our early races started in West Virginia, then the Philippines, Ohio, and then back home to Pittsburgh. We just finished our major outreach event — the Pittsburgh Marathon — where we recruited a PHenomenal Army of over 60 racers and volunteers, putting people all throughout the race in purple T-shirts — the color of PH Awareness. We had a ton of fun and generated a buzz as we spread the message about PH.

The team is now gearing up for our next event: Race Across the West in June. This year we compete as a two-woman team, racing from Oceanside, California to Durango, Colorado with a crew of eight people. As we prepare

for, and compete in this race, the PH community is joining us in the PHA Days of Unity campaign. The PH community continues to inspire us and we are excited to race with PH patients all over the country.

We invite you to race with us! There are many ways to be involved, from donating to our contribution to medical research to joining in our Team PH Ambassador program. To learn more about Team PHenomenal Hope, please check out our website at <http://teamphenomenalhope.org>. You can also like us on Facebook, or follow us on Twitter to keep up with the latest updates from the team.



State-of-the-Art Treatment of Acute Pulmonary Embolism



By **Belinda Rivera-Lebron, MD**



Phillip Lamberty, MD



Catalin Toma, MD

Venous thromboembolism (VTE) includes deep vein thrombosis (DVT) and pulmonary embolism (PE). It is the third most frequent cardiovascular disease, with an overall incidence of 100-200 per 100,000 individuals (1). VTE is responsible for the hospitalization of more than 250,000 patients annually in the United States (2).

Acute pulmonary embolism (PE) is the most serious presentation of VTE. PE is a potentially life-threatening disease and, in some cases, it presents as sudden death. Acute PE spans a wide spectrum of clinical outcomes, mainly based on the right ventricle's capacity to tolerate strain. Increased right ventricular (RV) afterload causes RV dilation that then incites cardiac ischemia, coronary hypoperfusion, and hypotension that can progress to cardiogenic shock.

Massive or high-risk PE is defined as an acute PE with sustained hypotension (systolic blood pressure less than 90 mm Hg for at least 15 minutes or requiring inotropic support) (3,4). In the International Cooperative Pulmonary Embolism Registry (ICOPER), the 90-day mortality rate for patients with high-risk PE at presentation was 52 percent (4-6). Hemodynamically stable patients with preserved RV size and function are classified as low-risk PE and have excellent prognosis once anticoagulation therapy is established (4).

There is an intermediate category, however, that warrants further discussion, as these patients may have an increased risk of 30-day mortality. Approximately one quarter of non-massive PE patients are categorized as submassive or intermediate-risk PE, using a risk stratification score based on clinical variables known as the pulmonary embolism severity index (PESI) (3). Within this category, risk delineation focuses on the presence of RV dysfunction (by echocardiography or CT angiography) and/or evidence of myocardial necrosis (by elevated cardiac biomarkers) (3,7). In patients who have evidence of both RV dysfunction and myocardial necrosis, 30-day mortality can reach 24.5 percent (8). Close monitoring of this group is recommended for early detection of hemodynamic decompensation and change in management.

Systemic thrombolysis, the recommended treatment for high-risk PE (3,4), improves hemodynamic parameters, reverses RV dysfunction, and improves survival in patients with acute PE; however it is associated with increased risk of major bleeding, including intracranial hemorrhage (9,10). In a recent study, in-hospital, all-cause mortality in hemodynamically unstable patients who received thrombolytic therapy was 15 percent, versus 47 percent without thrombolytic therapy (p less than 0.0001) (11).

The use of systemic thrombolysis for patients without hemodynamic compromise remains controversial. The recently published Pulmonary Embolism Thrombolysis (PEITHO) trial studied the role of fibrinolytic

The Acute PE Team at UPMC

We have assembled an Acute PE Team at UPMC to facilitate rapid consultation with clinicians experienced in the care of complex cases. It is a multidisciplinary team comprised of pulmonary and critical care physicians, vascular surgeons, interventional cardiologists, and cardiothoracic surgeons. We provide a rapid review of cases and recommendations from our multidisciplinary team to help in risk stratification and treatment of patients with acute PE (3,5). In addition to urgent consultations, our team meets on a monthly basis to review outcomes and continuously optimize our practice.

What services are offered by the Acute PE Team?

- Urgent inpatient consultations for patients with all types of PE
- Rapid coordination of multidisciplinary therapeutic recommendations that may involve pulmonary medicine, critical care medicine, interventional cardiology, vascular surgery, and cardiothoracic surgery
- State-of-the-art 24/7 capability for advanced techniques that include: catheter-directed thrombolysis, systemic thrombolysis, surgical embolectomy and hemodynamic support (ECMO)
- Monitoring of performance in the Acute PE and the Interventional PE QI Patient Databases
- Outpatient follow-up to monitor outcomes, including resolution of PE, recurrence, or progression into chronic thromboembolic pulmonary hypertension

How to consult the Acute PE Team

To refer a patient, facilitate a transfer to UPMC Presbyterian, or conduct a consultation, please call UPMC Medcall at 412-647-7000. The operator will connect you to the PE team pulmonologist on-call, who will help coordinate the care and involve additional team members as required.

therapy in patients with intermediate-risk PE (12). Its primary outcome, a composite of all-cause death or hemodynamic decompensation within seven days after randomization, was significantly reduced with thrombolysis (2.6 percent versus 5.6 percent; odds ratio 0.44; 95 percent CI 0.23-0.87; p = 0.02). However, an increased risk of major hemorrhage (6.3 percent versus 1.5 percent; p less than 0.001) and stroke (2 percent versus 0.2 percent; p = 0.003) was observed. An alternative strategy using reduced-dose tissue plasminogen activator (tPA) (50mg) in 121 patients with "moderate PE" reported no significant bleeding or differences in mortality (13). Current guidelines recommend against the routine use of systemic thrombolysis in these patients (3,14).

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Case Presentation: Catheter-Directed Thrombolytic Therapy for Pulmonary Embolism



By Roger A. Alvarez, DO, MPH

Pulmonary venous thromboembolism (PE) is a common and often life-threatening condition. Anticoagulation is the mainstay of therapy for most patients, with thrombolytic therapy historically reserved for patients with life-threatening hypotension or cardiac arrest. However, some patients remain at higher risk of morbidity and mortality, and recent studies have suggested a role for systemic or catheter-directed thrombolytic therapy in selected patients. We present a case of a patient who presented with an intermediate-risk PE who was successfully treated with catheter-directed thrombolytic therapy.

Case Report

A 59-year-old man with a history of chronic obstructive pulmonary disease (COPD) presented by emergency medical services (EMS) to another hospital with four days of progressively worsening and refractory shortness of breath, left-sided chest pain, and right leg swelling. On EMS arrival, his oxygen saturation was 60 percent on ambient air, and he was in moderate respiratory distress. He was placed on 15L/min of oxygen by a non-rebreather facemask and transported to the emergency department. There, his pulse was 105 beats per minute, blood pressure 130/80, and breathing 28 to 32 times per minute. A CT angiogram revealed extensive bilateral pulmonary emboli with evidence of right ventricular strain (Figure 1). His troponin and BNP were elevated at 0.16 ng/mL and 480 pg/mL, respectively. An echocardiogram confirmed a severely dilated right ventricle with severely decreased right ventricular systolic function, moderate pulmonary hypertension, and a highly mobile echodensity at the right ventricular side of the tricuspid valve with extension toward the right ventricular outflow tract (RVOT) consistent with a thrombus (Figure 2a). An ultrasound of his right lower extremity revealed deep vein thrombosis (DVT) in the popliteal and superficial femoral veins. He had an inferior vena cava (IVC) filter placed and unfractionated heparin was initiated.

His physicians consulted the PE team at UPMC for assistance, and he was ultimately transferred for further management of his pulmonary embolism.

On arrival at UPMC, he was tachycardic, normotensive, and required 10 L/min of oxygen by nasal cannula. Based on his combination of RV strain, elevated BNP and troponin, and severe hypoxia, as well as his age and underlying COPD, he was thought to have a high risk of morbidity and between 10 and 25 percent risk of death in 30 days based on his PE severity index (PESI) score. A multidisciplinary discussion of the PE team led to a recommendation for catheter-directed thrombolytic therapy.

The patient proceeded to the catheterization laboratory, where a pulmonary angiogram revealed significant bilateral clot burden (Figure 3). Right-heart catheterization revealed moderate pulmonary hypertension. EKOS EndoWave Infusion Catheters (EKOS Corporation, Bothell, Wash.) were placed into the pulmonary arteries and RVOT (Figure 4). He was treated with continued low dose intravenous heparin and a 12-hour infusion of tissue plasminogen activator (tPA). Over the subsequent few days, his oxygen requirement returned to his baseline of 4L/min by nasal cannula. A repeat echocardiogram showed reduced pulmonary pressures and improved RV function, as well as complete resolution of the RV thrombus (Figure 2b).

Conclusion

Some patients with PE who initially present with normal blood pressure remain at risk for later decompensation with complications, including cardiac arrest and death, despite therapy with anticoagulation. Recent studies have suggested that selected patients with this type of “submassive” or “intermediate-high risk” PE may benefit from a more aggressive treatment strategy, including pharmacomechanical catheter-directed therapy. This case highlights the possible benefit of this approach.



Figure 1. Axial (Panel A) and Coronal (Panel B) images from the thoracic CT angiogram that confirm the presence of bilateral large, acute, occlusive pulmonary embolism, with a greater clot burden in the right main pulmonary artery (solid white arrow).

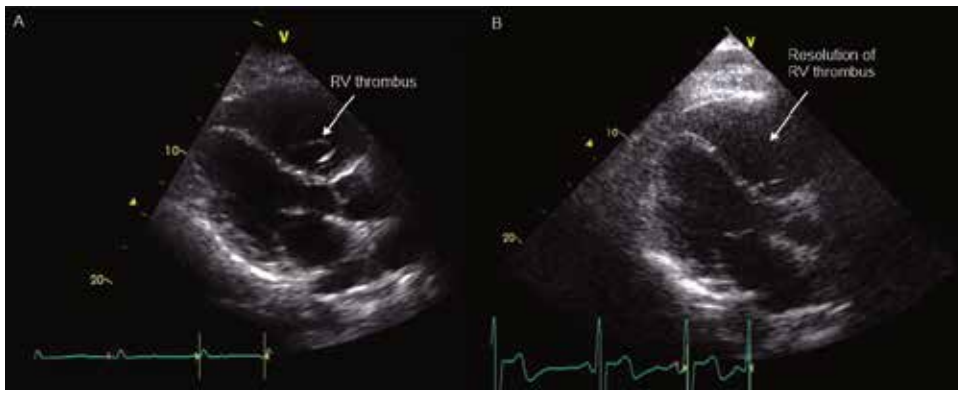


Figure 2. TTE revealed RV dilatation, an estimated pulmonary artery systolic pressure of 51 mmHg and a thin, serpiginous, highly mobile echodensity at the right ventricular side of the tricuspid valve with extension toward the right ventricular outflow tract (RVOT) consistent with a thrombus that was 3.5 cm x 0.3 cm in size (Panel A). After tPA, the thrombus was no longer visible (Panel B).



Figure 3. PA angiogram revealed poor perfusion to a large region of the RLL and a hazy filling defect in the right lower lobar PA consistent with a large PE.



Figure 4. EKOS catheters in place in the bilateral PA. A 6 cm catheter extends into the RLL artery, and an 18 cm catheter extends distally into the LLL artery, and proximally reaches the RVOT, in an effort to provide lysis for the RV thrombus in addition to the PE.

Progression of Pulmonary Embolism: Chronic Thromboembolic Pulmonary Hypertension



By Patricia George, MD

In most cases, pulmonary thromboembolism resolves completely after treatment with anticoagulation, and patients are able to return to their previous quality of life. However, approximately 0.1-0.5 percent or more of patients who survive PE go on to develop chronic thromboembolic pulmonary hypertension (CTEPH) (1). In a single-center, prospective study of patients who had PE and developed symptomatic CTEPH, the cumulative incidence was reported at 3.8 percent at two years (2). If we extrapolate these data, the numbers could be almost 20,000 cases per year. Furthermore, in another study, it was found that in patients diagnosed with CTEPH, as many as 25 percent had no known previous history of PE (3). In the case of CTEPH, making a timely and accurate diagnosis is critical, as this disease can potentially be cured at a center that specializes in pulmonary thromboendarterectomy (PTE).

The most important aspect in caring for patients with CTEPH is making the diagnosis. It is important to maintain a low index of suspicion for pulmonary hypertension (PH) in patients who have been treated for PE, as well as for CTEPH in patients newly diagnosed with PH, and investigate promptly when this may be the case.

Patients with CTEPH manifest similarly to patients with pulmonary hypertension due to other causes. Symptoms include dyspnea on exertion, fatigue, palpitations, light-headedness, syncope, and cough. As the disease progresses, patients also may have edema. Often the disease is indolent and diagnosis can be delayed.

Diagnosis

When CTEPH is suspected, the most sensitive diagnostic test is the ventilation/perfusion scan (V/Q scan). This is considered the gold standard and is more sensitive than CT angiogram as a screening test for CTEPH(4). To evaluate for pulmonary hypertension, an echocardiogram is often performed as a screening test, followed by a confirmatory right-heart catheterization.

Treatment

Once the diagnosis of CTEPH is made, the next question becomes that of operability. Patients must be healthy enough from a comorbidity standpoint to undergo PTE and also have disease that is reachable by surgical techniques. To assess these factors, the patient meets with the CTEPH clinician and surgeon for a thorough history and physical, as well as review of the medical record and testing. To assess the anatomy of the thromboemboli, centers may use pulmonary angiography, or now, with advanced techniques, high-resolution CT angiography. Based on these tests, a recommendation is made as to whether the patient would benefit

from PTE. After discussion with and education of the patient, the decision is made whether to undergo surgery. Importantly, in cases where the patient is deemed operable, it is recommended not to delay surgery — definitive treatment — for a trial of medical therapy.

PTE is a procedure performed on cardiopulmonary bypass, where the patient is cooled and undergoes short periods of circulatory arrest to allow complete clot removal from the pulmonary arteries. At experienced centers, this procedure is associated with low mortality (less than 5 percent). Upon completion, the patient is slowly warmed and monitored very closely post-operatively, as the early period poses a risk for ischemia-reperfusion injury. Patients are usually in the hospital for seven to 10 days for the entire procedure, and then an echocardiogram and V/Q scan are performed before discharge. Patients are usually recommended lifelong anticoagulation after PTE.

Recovery

Often patients leave the hospital without the need for oxygen, but it is not unusual to take longer to fully recover lung function post-PTE. We follow up with patients routinely at one-month and at three-months surgically and then medically after that to assure complete resolution of PH. In cases where there is residual or refractory PH, there is now an FDA-approved medication, riociguat, for this indication as well as for inoperable CTEPH.

The UPMC Approach

At UPMC, our multidisciplinary CTEPH Team works closely with the patient and referring physician to thoroughly evaluate the patient's disease and recommend a treatment plan.

We offer timely assessment as well as novel testing, including pre-operative exercise echocardiography and right-heart catheterization, and post-operative follow up with similar testing to document resolution of disease. We have performed more than 25 cases with excellent results. Physicians in the comprehensive pulmonary hypertension program will continue to follow patients to assure optimal treatment regimens and the best outcomes possible.

To refer a patient for CTEPH evaluation, please call 1-877-PH4-UPMC (1-877-744-8762) or email us at PHprogram@upmc.edu.

For a list of references to this article, other articles in this issue, and the Division of PACCM's recent publications and suggested reading for this issue, visit UPMCPHysicianResources.com/Pulmonology.

State-of-the-Art Treatment of Acute Pulmonary Embolism *(continued)*

The use of catheter-directed thrombolysis is emerging as an effective alternative in patients with intermediate or high-risk PE, using small doses of a thrombolytic agent (15). In a randomized, controlled clinical trial of 59 intermediate-risk patients, heparin plus ultrasound-guided catheter-directed thrombolysis was compared to heparin alone (16). Ultrasound-guided catheter-directed tPA significantly reversed RV dilatation at 24 hours by echocardiogram, without an increased risk of bleeding.

For intermediate or high-risk PE, surgical embolectomy may be an alternative, especially if thrombolysis is contraindicated or has failed. A perioperative mortality of less than 6 percent has been reported for

embolectomy before hemodynamic collapse (17). Extracorporeal membrane oxygenation (ECMO) may rescue those in critical situations, ensuring circulation and oxygenation until definitive management is provided.

For a list of references to this article, other articles in this issue, and the Division of PACCM's recent publications and suggested reading for this issue, visit UPMCPHYSICIANRESOURCES.COM/PULMONOLOGY.

Educational Opportunities

PACCM is deeply committed to a mission that includes:

- Providing the highest-quality compassionate patient care for patients with lung disease
- Mentoring and training medical students, residents, fellows, and young faculty
- Research and scientific discovery

To foster an educational and collaborative environment, the division offers the following weekly conferences throughout the academic year:

Basic and Translational Research in Lung Disease Conference is held every Tuesday from noon to 1 p.m. in the Biomedical Science Tower, Conference Room 1295. This conference provides pulmonary faculty and staff an opportunity to hear speakers from throughout the university outline their current biomedical research efforts in order to facilitate expanded collaborations.

Pulmonary Case Conference is held every Thursday from noon to 1 p.m. in the Biomedical Science Tower, Conference Room 1295.

Pulmonary Grand Rounds are held each Friday from noon to 1 p.m. in UPMC Montefiore, Conference Room NW628. It consists of lectures by external and internal speakers and is designed to bring forth the latest scientific and clinical developments in pulmonary and allergic diseases.

If you wish to be placed on our email distribution list, please contact Theresa Dobransky at dobranskyta@upmc.edu.

How to Refer a Patient for Lung Transplant Evaluation

To refer a patient for lung transplant evaluation, the following information is needed:

- Patient's name and contact information
- Date of birth
- SSN
- Insurance information
- Medical records, including an H&P, PFTs, CT scan, and CXR reports from the last two years, routine blood work results, current medication list, and any cardiac testing that has been done, such as an echo and/or left- and right-heart catheterization

The information can be faxed or mailed to the attention of Nancy Pepke, BSN, RN, CCTC, intake coordinator:

Fax: 412-648-6369

Mailing address:

UPMC Presbyterian
Lung Transplant Program
200 Lothrop St., Suite C-900
Pittsburgh, PA 15213

Insurance clearance can take up to two to three weeks. Once insurance authorization is received and medical records have been reviewed, the patient will be contacted for a phone interview/history. Once deemed acceptable for evaluation, the patient will be asked to provide a date when he or she AND a family member can come in for three to five days of testing. Referring physicians can request an expedited schedule for a patient based upon their assessment. If you have questions, please call the pretransplant office at **412-648-6202**.

Case Presentation: Persistent Dyspnea on Exertion in a Young Woman After PE



By Jennifer H. Keeley, DNP, MSN, ANP-BC

Chronic thromboembolic pulmonary hypertension (CTEPH) is defined as pre-capillary pulmonary hypertension (PH) in the presence of chronic thromboembolic disease. CTEPH is the only type of PH that is potentially curable by a surgical procedure: pulmonary thromboendarterectomy (PTE). It is crucial to recognize the importance of early referral of any patient who may have CTEPH, even in the absence of resting pulmonary hypertension, as excellent results can be achieved by reducing exercise-induced PH and restoring pulmonary vascular anatomy.

Case Report

The patient is a 28-year-old, previously healthy woman who presented with chest pain and dyspnea on exertion three weeks after a motor vehicle accident and was diagnosed with acute pulmonary embolism. She was anticoagulated with heparin then warfarin, and eventually switched to rivaroxaban due to difficulty maintaining a consistent therapeutic INR on warfarin. Although her chest pain improved, it did not completely resolve, and she had persistent dyspnea with activities of daily living. She also experienced profound fatigue. This persistent dyspnea limited her ability to work at her physically demanding job at the local tree nursery.

Her past medical history was noncontributory. Her family history was positive for deep vein thrombosis in her father. Her coagulation panel showed evidence of lupus anticoagulant.

After her initial evaluation in the pulmonary hypertension clinic, the patient had a screening ventilation/perfusion (V/Q) scan that showed an absence of perfusion in the right middle and lower lobes (Figure 1) and was consistent with filling defects found on CT angiogram (Figure 2). Her echocardiogram showed borderline pulmonary hypertension with an estimated right ventricular systolic pressure 41 mmHg. To confirm the diagnosis, she underwent an exercise right-heart catheterization, which revealed an increase in mean pulmonary artery pressure from 23 mmHg to 39 mmHg at maximal exercise. The patient underwent successful pulmonary thromboendarterectomy and mitral valve repair to remove fibrous vegetations.

Her symptoms have improved postoperatively. Her postoperative echocardiogram showed an estimated pulmonary artery systolic pressure of 28 mmHg. She is currently enrolled in cardiac rehabilitation and improving her exercise capacity weekly. She is maintained on rivaroxaban.

Discussion

Pulmonary emboli fail to resolve with anticoagulation in up to 3 percent of patients (1). This case highlights several key points in the presentation, diagnosis, and management of CTEPH. Her presentation was consistent with indolent symptoms in CTEPH (persistent dyspnea on exertion, chest pain, exercise intolerance, and fatigue). Other symptoms include lightheadedness and palpitations. As CTEPH progresses, so do symptoms related to right-heart dysfunction such as edema or syncope (2). While our patient had an insidious progression, people with CTEPH may also experience episodes of acute progression. As for her diagnosis, the first confirmatory study performed was the V/Q scan. This is the test of choice in screening for chronic thromboembolic disease. Although many providers are using a CT angiogram to screen for CTEPH, studies show this test can actually miss chronic disease. It has been reported that CT is not as sensitive for detecting CTEPH as a V/Q scan (51.3 percent sensitivity for CT versus 90–100 percent sensitivity for V/Q) (3). She also had a CT angiogram to define her thromboembolic anatomy for surgical planning. Interestingly, her echocardiogram at rest showed borderline PAH, and due to the fact that she had exercise-induced symptoms, an exercise-induced right-heart catheterization was performed and was crucial in making the diagnosis. Once the diagnosis was made, she was scheduled for the definitive treatment, pulmonary thromboendarterectomy. She will continue to be followed postoperatively for improvement in her symptoms, and if she has residual pulmonary hypertension, medical therapy will additionally be considered.

Conclusion

This case not only highlights the importance of early recognition of CTEPH but also the importance of early referral to a specialist center experienced in the assessment and surgical management of this potentially curative disease. Surgical decision-making involves many factors: comorbid conditions, accessibility of diseased vessels, and the correlation of clot burden to hemodynamic impairment.

For a list of references to this article, other articles in this issue, and the Division of PACCM's recent publications and suggested reading for this issue, visit UPMCPhysicianResources.com/Pulmonology.

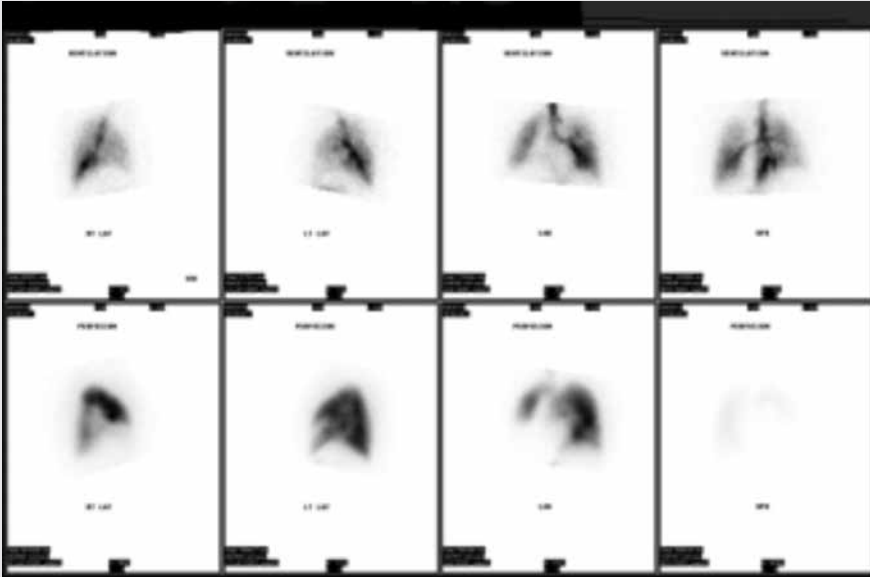


Figure 1. Ventilation/Perfusion(V/Q) scan showing an absence of perfusion in the right, middle, and lower lobes.



Figure 2. CT angiogram showing filling defects.

New Pulmonary Hypertension Clinical Trials and Research Studies

Current Pulmonary Hypertension Clinical Trials that are currently open for enrollment at the University of Pittsburgh:

Study Name: RISE-IIP

PI: Michael Risbano, MD, MA

Coordinator: Pamela M. White, RN, BSN, CCRC
(412-624-3147, whitepm@upmc.edu)

Summary: A randomized, double-blind, placebo-controlled phase II study to determine efficacy and safety of riociguat in patients with symptomatic pulmonary hypertension associated with idiopathic interstitial pneumonias (IIP).

Study Name: VAST

PI: Michael Risbano, MD, MA

Coordinator: Cathy Kessinger, RN and Dani Camp, RN

Summary: To evaluate the prevalence of pulmonary hypertension in the COPD or HIV-infected population who have elevated NT-ProBNP levels and/or abnormal echocardiograms and/or DLCO less than 60 percent predicted.

Study Name: Inhaled Nitrite

PI: Marc Simon, MD, MS, FACC

Coordinator: Pamela M. White, RN, BSN, CCRC
(412-624-3147, whitepm@upmc.edu)

Summary: A single-center, open label phase II study to evaluate the effect of inhaled nitrite delivered in a dose escalation manner on the change in pulmonary vascular resistance (PVR) in subjects with Group II or III pulmonary hypertension undergoing right-heart catheterization.

Study Name: Arena

PI: Marc Simon, MD

Coordinator: Jessica Pisarcik, RN
(412-647-4463, pisarcikje2@upmc.edu)

Summary: An open-label pilot study followed by a double-blind, randomized, parallel-group, placebo-controlled phase 2 trial of APD811, an oral IP receptor agonist, in patients with PAH.

Study Name: REPAIR TRIAL

PI: Marc Simon, MD

Coordinator: Kristin Shoemaker, RN
(412-692-2769, shoeka@upmc.edu)

Summary: A prospective, multicenter, single-arm, open-label, phase IV study of the effects of macitentan on right ventricular remodeling in pulmonary arterial hypertension assessed by cardiac MRI.

Study Name: GS-US-357-1394

PI: Marc Simon, MD

Coordinator: Kristin Shoemaker, RN
(412-692-2769, shoeka@upmc.edu)

Summary: Phase 2, dose-ranging, placebo-controlled, double-blind study to evaluate the effect of GS-4997 (an inhibitor of apoptosis signal-regulating kinase 1, ASK1) on pulmonary vascular resistance (PVR), as measured by right-heart catheterization (RHC) in subjects with pulmonary arterial hypertension (PAH).

Study Name: The BEAT Trial

PI: David Ishizawar, MD

Coordinator: Kristin Shoemaker, RN
(412-692-2769, shoeka@upmc.edu)

Summary: A multicenter, double-blind, randomized, placebo-controlled, phase 3 study to assess the efficacy and safety of oral BPS-314d-MR added on to treprostinil, inhaled (Tyvaso®), in subjects with pulmonary arterial hypertension.

Study Name: SYMPHONY

PI: David Ishizawar, MD

Coordinator: Kristin Shoemaker, RN
(412-692-2769, shoeka@upmc.edu)

Summary: A multi-center, open-label, single-arm, phase 3b study of macitentan in patients with PAH, to psychometrically validate the PAH-SYMPACT instrument.

Study Name: TDE 310/311

PI: Mike Mathier, MD

Coordinator: Kristin Shoemaker, RN
(412-692-2769, shoeka@upmc.edu)

Summary: A phase III, international, multi-center, randomized, double-blind, placebo-controlled, event-driven study to compare the time to first clinical worsening in subjects with PAH receiving UT-15C in combination with a PDE5-I or ERA compared with a PDE5-I or ERA alone.

Save the Date:

Munich-Pittsburgh Lung Conference 2015

The annual Pittsburgh International Lung Conference was established in 2002 with the objective to provide cutting-edge clinical, translational, and basic investigations in specific areas of lung disease.

In 2014, we initiated a partnership with the Comprehensive Pneumology Center, Institute of Lung Biology and Disease, Ludwig-Maximilians University and Helmholtz Zentrum München, Munich, Germany, to co-host the conference and establish a wider collaboration for clinical and research development.

As part of that alliance, this year's Lung Conference, Precision Medicine: From Molecular Mechanisms to Targeted Therapy, will take place in Munich, Germany, on October 2-3, 2015.

For information regarding oral presentations, poster sessions, and abstract submission deadlines, please be sure to check the conference website at <http://www.mlc2015.de/>

Conference Recap — Management of Acute and Chronic PE

On Friday, March 20, the Division of Pulmonary, Allergy, and Critical Care Medicine (PACCM) hosted the Spring Clinical Conference: Management of Acute and Chronic Pulmonary Embolism. This was a clinician-centered conference addressing recent advancements in treating acute pulmonary embolism (PE) and chronic thromboembolic pulmonary hypertension (CTEPH). In his keynote address, Dr. Donald Yealy, chairman of Emergency Medicine, shared his frontline perspective about current consequences of our technologies, including overdiagnosis, stressing the importance of incorporating pre-test probability into our diagnostic algorithm to avoid unnecessary testing. He also shared experience in the outpatient treatment of low-risk patients with acute PE, a thought-provoking concept that may help lower hospitalization and health care costs.

In her talk about classification and risk stratification in massive and submassive PE, Dr. Belinda Rivera-Lebron discussed current guidelines and treatment algorithms in the management of acute PE. Venous thromboembolism (PE and deep vein thrombosis) affects between 300,000 and 600,000 Americans each year, and carries a 10–20 percent mortality rate within one month. Our goal is to rapidly stratify patient risk in an effort to better triage patients at the time of PE diagnosis and prevent chronic complications.

Vascular surgeon Dr. Rabih Chaer discussed the interventional approach in the management of submassive PE, reviewing the recent literature and sharing the UPMC experience in ultrasound-assisted and non-ultrasound assisted catheter-based lysis. Early randomized controlled studies in catheter-directed interventions have shown more rapid reversal of RV dilation compared to heparin alone, providing a basis for further investigations in this treatment modality. Questions remain regarding which patients with submassive PE most benefit from catheter-directed therapy, as well as whether such therapy impacts long-term outcomes.

Dr. Franklin Bontempo then provided a thorough summary of the new oral anticoagulants, discussing when to use them, their advantages, and the disadvantages of these treatments. Dr. Arthur Boujoukas and Dr. Catalin Toma hosted a lively discussion contrasting standard-of-care anticoagulant therapy versus catheter-based thrombolysis. Dr. Patricia George and Dr. Tom Gleason rounded out the afternoon speaking on the chronic complications of PE: Chronic Thromboembolic Pulmonary Hypertension (CTEPH). This is an often unrecognized complication of acute pulmonary embolism, with an incidence close to 4 percent or higher within two years after PE. Dr. George emphasized the importance of V/Q scan in the screening of chronic thromboembolic disease, and Dr. Gleason discussed pulmonary thromboendarterectomy, which is potentially curative in this disease.

We want to thank all who attended and engaged with us in fascinating discussion on this timely topic and look forward to updates in the future. The conference proceedings will be published online in a UPMC video series for online CME, as well as in the *PulmCCM Journal*.

For more information about our Acute and Chronic PE Programs, please go to our website at UPMC.com.

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For a list of references to this article, other articles in this issue, and the Division of PACCM's recent publications and suggested reading for this issue, visit UPMCPHYSICIANRESOURCES.COM/PULMONOLOGY.

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