



Pulmonary Advances

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WINTER 2015

New Program Delivers Integrated, Gender-specific Care for Women with Pulmonary Diseases

The new Women's Lung Health Program at Brigham and Women's Hospital (BWH) provides advanced multidisciplinary care and tailored disease management for women with respiratory disease, including asthma, chronic lung infections, chronic obstructive pulmonary disease (COPD), dyspnea, lymphangioleiomyomatosis (LAM), lung cancer, pulmonary hypertension, and vocal cord dysfunction.

"Sex differences in diseases are widespread and can influence risk, prevalence, severity, treatment response, and many other aspects related to evaluation and management of disease," said Paula A. Johnson, MD, MPH, Executive Director of the Connors Center for Women's Health and Gender Biology at Brigham and Women's Hospital. "Gender-specific approaches to care and research to better understand the underlying biological differences in diseases in men and women are critical to improving outcomes in all patients."

The Women's Lung Health Program brings together clinicians and researchers with vast clinical expertise and research interests in lung disease in women, including pulmonologists, pulmonary vascular specialists, thoracic surgeons, laryngologists, infectious disease specialists, geneticists, medical on-



Elizabeth Henske, MD, Director, Center for LAM Research and Clinical Care and Co-director of the Pulmonary Genetics Center, is part of a multidisciplinary team of specialists in the new Women's Lung Health Program at BWH which provides advanced care and tailored disease management form women with respiratory diseases.

cologists, dietitians, and additional specialists as needed to address the unique aspects of lung diseases in women.

Specific areas of focus for the Program include:

Asthma – Although in childhood more boys than girls have asthma, in adulthood asthma is predominantly a disease of women. Women face unique challenges managing their asthma, whether related to peri-menstrual asthma, asthma in pregnancy, or post-menopausal changes in their disease and its management. Megan Hardin, MD, a pulmonologist, respiratory epidemiologist, and member of Partners Asthma Center, has forged a close collaboration with obstetricians in BWH's maternal-fetal medicine group to provide expedited, coordinated care for pregnant women with asthma (see *Case Study on back cover*). Together with BWH pulmonologist Barbara Cockrill, MD, and Christopher H. Fanta, MD, Director of

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Real-time Image-guided Video-assisted Thoracic Surgery Procedures Help to Remove Small Lung Cancers Less Invasively

Led by Raphael Bueno, MD, Chief of Thoracic Surgery at Brigham and Women's Hospital (BWH) and thoracic surgeon in the Center for Thoracic Oncology at Dana-Farber/Brigham and Women's Cancer Center, a multidisciplinary team developed and performed some of the first real-time image-guided video-assisted thoracic surgery (iVATS) wedge resections in the U.S.

Performed in the Advanced Multimodality Image Guided Operating (AMIGO) suite at BWH, iVATS lung resection combines video-assisted thoracic surgery (VATS) with real-time intraoperative computed tomography (CT)-fluoroscopy imaging. VATS is part of the standard of care in excising lung tumors, however, localization of the tumor in the operating room typically relies on previous diagnostic CT imaging and palpation of the lung. Subsequent surgical resection with this approach can result in the removal of more normal functioning surrounding lung tissue than desired to achieve clear margins.

The iVATS procedure is part of an AMIGO clinical trial, developed and led by Dr. Bueno in collaboration with radiologist Ritu R. Gill, MD, MPH, and research scientist Jayender Jagadeesan, PhD, at Harvard Medical School, and employs real-time intraoperative CT imaging of the lung combined with video technology to locate and mark the tumor using intraoperative imaging-guidance so that it could be reliably resected with the minimally of lung tissue lost.

With the lung inflated, the tumor is marked with a metallic bar that is positioned through a needle and connected to a suture. This simple device can precisely locate and track the lesion using X-ray imaging. After the lung is deflated this bar lodges in the tissue, guiding the surgeon to the precise location of the tumor. The iVATS approach is particularly useful in locating small tumors, which can be difficult to palpate and allows limited resections with adequate margins. Since the completion of the first iVATS procedure, a total of 23 patients underwent this procedure in the Advanced Multimodality Image Guided Operating Suite (AMIGO) as part of a now completed clinical trial.

"This application is designed to improve thoracic surgery techniques and lung cancer treatments," said Dr. Bueno. "While similar approaches have been used in the excision of breast tumors, and metal wires and coils have been used to identify lung nodules, the intraoperative use of these specialized sutures with real-time radiological imaging in the treatment of lung cancer is both innovative and game-changing. It is like moving from using maps to plan a journey to using GPS."



Brigham and Women's Hospital surgeons perform image-guided Video-assisted Thoracic Surgery (iVATS) procedures in the AMIGO suite.

About the AMIGO Suite

The AMIGO suite is a fully integrated operating suite, offering immediate intra-procedural access to an extensive range of advanced imaging modalities. This facility is part of the National Institutes of Health funded National Center for Image Guided Therapy (P41-NIBIB, Drs. Jolesz and Tempany, Co-Principal Investigators). The 5,700 square foot space is divided into three interconnected procedure rooms housing real-time anatomic, functional, and molecular imaging modalities, including MRI, PET/CT, CT-fluoroscopy, and ultrasound. Specialists at Dana-Farber/Brigham and Women's Cancer Center are collaborating to introduce novel image-guided techniques in AMIGO in order to advance diagnosis and treatment for many forms of cancer, including malignant tumors of the brain, prostate, kidney, liver, lung, adrenal gland, bone, cervix, vagina, and uterus.



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View a Video Introduction to the AMIGO Suite at BWH
www.brighamandwomens.org/amigo

Improving Outcomes for Patients with Pulmonary Embolism and Chronic Thromboembolic Pulmonary Hypertension

Specialists in vascular medicine, pulmonary medicine, emergency medicine, critical care, cardiothoracic surgery, interventional cardiology, and thoracic imaging in the new Acute Pulmonary Embolism (PE) Program at Brigham and Women's Hospital (BWH) are collaborating to provide rapid assessment, triage, and management for patients presenting with signs and symptoms of acute pulmonary embolism.

"Pulmonary embolism is the third most common cause of cardiovascular death in the United States with at least 180,000 fatalities annually, and the incidence of PE appears to be rising," said Mark Creager, MD, Co-director of the Acute PE Program.

Rapid Response in Acute Pulmonary Embolism

The Acute PE Program provides patients presenting with suspected acute PE rapid assessment and systematic multidisciplinary care delivered through an integrated program, as well as coordination of multidisciplinary follow-up care after discharge. Patients who present to the Emergency Department (ED) at BWH undergo immediate evaluation by ED staff, who utilize a single pager to activate the Acute PE Program team if PE is detected. Transfers from an outside ED with detected PE or transfers with unstable or high-risk PE from outside hospitals are triaged to the BWH ED or directly to the Shapiro Cardiovascular Center, respectively.

"After an expedited multidisciplinary evaluation, we deliver advanced services tailored to the underlying condition and diagnosis," said Aaron B. Waxman, MD, PhD, Co-director of the Acute PE Program and Medical Director of the CTEPH Program. "Many times, patients arrive to us with symptoms of acute pulmonary embolism that have not responded adequately to therapy and are ultimately found to have chronic thromboembolic pulmonary hypertension or another pulmonary condition. Our goal in establishing this Program is to assign patients to the most appropriate therapy as quickly as possible in order to improve outcomes."

Treatment approaches used in patients with acute PE range from intensive anticoagulation, including the non-vitamin-K oral anticoagulants if appropriate, and systemic thrombolytic therapies to catheter-based low-dose thrombolysis and surgical embolectomy. Rapid assessment by the multidisciplinary team and state-of-the-art imaging are employed to choose the most appropriate therapy for each patient. In patients found to have chronic thromboembolic pulmonary hypertension (CTEPH), pulmonary thromboendarterectomy or balloon pulmonary artery angioplasty are performed in appropriate cases.



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Brigham and Women's Hospital Video Education Center

Videos from Our Experts on Pulmonary Topics

The Brigham and Women's Hospital Video Education Center offers a wide range of educational resources for physicians and other health care professionals. The Center features several videos relating to pulmonary conditions, including:

- Women and Lung Cancer
- LAM: From Puzzle to Treatment
- Low Dose CT Scanning for Lung Cancer
- Pulmonary Hypertension in Sickle Cell Disease
- Robotic Lobectomy
- VATS Right Upper Lobectomy

Case Study:

Chronic Thromboembolic Pulmonary Hypertension

Background:

A 44-year-old female was transferred to Brigham and Women's Hospital with a history of CTEPH and deep vein thrombosis (DVT). She presented with progressive shortness-of-breath and right heart failure. On admission, she underwent a comprehensive evaluation, including pulmonary angiography and echocardiography (Figure 1).

Findings were consistent with severe pulmonary arterial hypertension (PAH) with mPA 52 mm Hg and a PCWP of 6 mm Hg. The cardiac index was severely reduced at 1.94 l/min/m² and the PVR markedly elevated at 1092 dynes. Following inhaled nitric oxide, there was no reduction in PA pressure. Proximal thrombus in the right main artery was evident on preoperative PE-protocol CT (Figure 2). It appeared chronic. On full pulmonary angiography, there was clear cut off of the right middle lobe perfusion and early cut off and incomplete filling of the right upper lobe. Luminal defects involving the left upper lobe also were noted. These findings were consistent with CTEPH bilaterally.

Approach:

After the team discussed and formulated short- and longer-term plans, targeted oral medical therapy with pulmonary vasodilators was started for pulmonary arterial hypertension components of the patient's CTEPH. She was counseled on surgery to improve symptoms and underwent a pulmonary thromboendarterectomy at BWH. At surgery, a large amount of thromboembolic material was removed from almost every branch of the right and left pulmonary arteries. Right ventricle function improved at the end of the procedure.

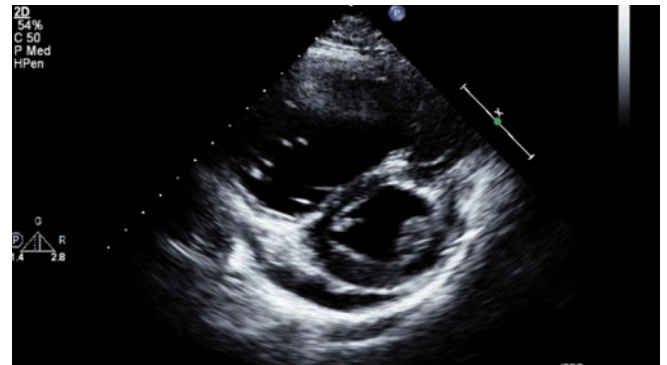
Follow up:

At three weeks after surgery, the patient's shortness-of-breath had resolved. An echocardiogram (Figure 3) showed a less-dilated right ventricle, normalization of the interventricular septum, and resolution of the pericardial effusion. The estimated pulmonary artery systolic pressure had normalized.

Access and Information

For a consultation, more information on our pulmonary services, or to refer a patient to the Acute PE Program, please call our helpful and experienced Referral Coordinators at (617) 732-9894 or email bwhreferrals@partners.org.

Figure 1



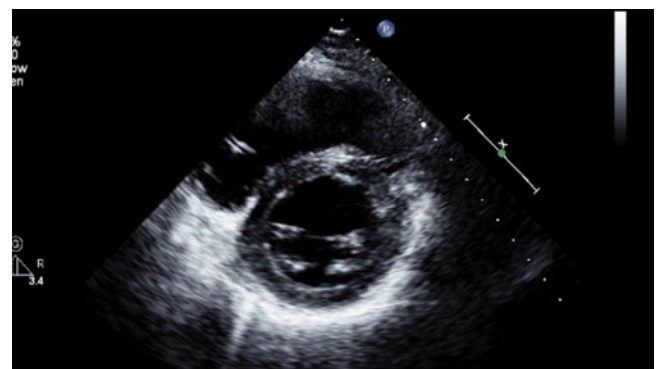
Preoperative echocardiogram shows a dilated right ventricle, flattening of the interventricular septum, and a moderate pericardial effusion.

Figure 2



Preoperative PE-protocol CT scan showing thrombus with some evidence of webbing in the right main pulmonary artery and within a segmental branch. Thrombus also can be seen within the lower lobe branch of the left pulmonary artery and within a sub-segmental branch of the left pulmonary artery.

Figure 3



Post-operative echocardiogram shows less dilated right ventricle, normalization of the interventricular septum, and resolution of the pericardial effusion. The estimated pulmonary artery systolic pressure had normalized.

New Program Delivers Integrated, Gender-specific Care for Women with Pulmonary Diseases...

continued from front cover

Partners Asthma Center, Dr. Hardin is providing care for asthmatic women throughout their lifespan. Care of patients with complex or refractory disease can draw on the expertise of colleagues in allergy, ENT, gastroenterology, cardiology, and endocrinology to provide multidisciplinary expertise and coordinated care. Researchers at BWH are investigating genetic, hormonal, and environmental exposure differences that may explain the differential expression of asthma in women. Dr. Hardin also is exploring the interface between asthma and COPD (*Eur Respir J* 2014; 44:341-50).

Chronic Obstructive Pulmonary Disease (COPD) – Chronic obstructive pulmonary disease has now become the third leading cause of death in the United States, and since 2000, more women than men have died from COPD. Women face unique challenges in the diagnosis and management of COPD. Women with COPD are more likely to be diagnosed with asthma. On average, they have different symptoms than men, including more shortness of breath, and report worse quality of life. Women appear to be more sensitive to tobacco smoke, as measured by lung function. The reasons for the differences are not well understood and may include genetics, biology, environmental factors and lifestyle. Dawn L. DeMeo, MD, MPH, and Dr. Hardin, pulmonologists within the Channing Division of Network Medicine, are currently investigating the biological underpinnings of these differences, with an aim to improve COPD detection and treatment and improve outcomes for women with COPD.

Lung Cancer in Women – Because women are more susceptible to certain types of lung cancer, have higher rates of lung cancer as non-smokers, and carry certain tumor-specific genetic mutations, dedicated care and research for women with lung cancer is essential in improving outcomes and better understanding the underlying pathophysiology of the disease. Thoracic surgeon Yolonda L. Colson, MD, PhD, has dedicated years to investigating and treating lung cancer in women and striving to improve outcomes in all patients. As Director of the Women's Lung Cancer Program at Dana-Farber/Brigham and Women's Cancer Center, she is leading research evaluating ways to better stage lung cancer, including new techniques to identify lymph nodes at risk for metastases (*J Thorac Cardiovasc Surg* 2013; 146:562-70). She also is exploring genetic clues to susceptibility to lung cancer and severity of the disease, as well as possible ways to use that information in patient care.

Lymphangiomyomatosis – Led by Elizabeth Henske, MD, Director, and Souheil Y. El-Chemaly, MD, Medical Director of the Center for LAM Research and Clinical Care at BWH, care for women with LAM at BWH emphasizes aggressive multidisciplinary approaches to diagnosis and treatment, including lung transplantation in select cases. Researchers in the Center

are investigating combination therapies designed to offer a lasting response after initial treatment. A current clinical trial (*Safety Study of Sirolimus and Hydroxychloroquine in Women With Lymphangiomyomatosis*) is evaluating the safety of sirolimus and hydroxychloroquine in patients with LAM. Researchers at BWH also are leading ongoing biomarker studies for LAM using a dedicated biorepository of blood samples from LAM patients and are investigating the role of estrogen in LAM.

Pulmonary Hypertension – Women have up to seven times the risk of developing idiopathic pulmonary hypertension (PH) than men and generally exhibit symptoms up to ten years earlier than men. They also are at higher risk for autoimmune disorders that are associated with the development of PH, such as lupus and rheumatoid arthritis. Pulmonary vascular specialists Barbara Cockrill, MD, and Aaron Waxman, MD, PhD, offer highly-specialized care for women with pulmonary hypertension and unexplained dyspnea and collaborate closely with other specialists, including vascular medicine specialists, cardiac surgeons, rheumatologists, and others, in the care of patients. Clinical trials of novel approaches to PH include new oral drugs that may serve as alternatives to intravenous medications, as well as expanded indications for FDA-approved classes of drugs. Innovative diagnostic testing includes invasive cardiopulmonary exercise testing to identify the underlying cause of unexplained symptoms and inform patient care.

Voice and Vocal Cord Dysfunction – Paradoxical vocal fold motion (PVFM), known to impact more women than men, is diagnosed and treated using a team approach, including laryngologist Jayme Dowdall, MD, Co-director of the Voice Program at BWH, and voice pathologist Chandler Thompson, DMA, MS, CCC-SLP, as part of the Women's Lung Health Program. PVFM leads to paradoxical closure of the vocal folds during breathing. Strategies to treat PVFM include decreasing sources of laryngeal irritation and the use of special breathing techniques. Because asthma often coexists or is mistaken for PVFM, these specialists collaborate closely with pulmonologists in the Program to develop treatment approaches best suited for each patient. Other voice-related conditions treated by specialists in the Voice Program include phonotraumatic lesions and idiopathic subglottic stenosis, which also are more common in women than men.

Case Study on back cover

Access to Our Pulmonary Services

At Brigham and Women's Hospital, our pulmonary specialists are available for timely consultations and will work with you to develop treatment plans for your patients. Our Physician Liaison Ellen Steward can provide direct assistance with patient referrals and consultations. Ellen can be reached at (617) 582-4733 or via email at esteward@partners.org.

Case Study: Asthma and Pregnancy

Background:

A 37-year-old female patient (G2P1), who was 12 weeks pregnant and had a history of severe persistent asthma, was referred by her obstetrician for worsening shortness of breath, chest tightness, and wheezing.

Her asthma had begun eight years ago during her first pregnancy and was difficult to control throughout that pregnancy, with multiple hospitalizations for worsened asthma and one hospitalization for pneumonia. She has been treated with fluticasone-salmeterol combination inhaler, montelukast, and an albuterol rescue inhaler used as needed. As often as twice per year she has needed oral corticosteroids for flares of her asthma. Allergy skin testing was negative. She has chronic rhinitis and post-nasal drip, worse during this second pregnancy.

Her daughter developed an upper respiratory tract infection approximately one week ago. During the week prior to her visit, the patient had been using her albuterol inhaler two-to-three times per day and found it difficult to sleep because of cough and shortness of breath. Her peak expiratory flow, normally maintained at approximately 350 L/min, was 220 L/min on the day of referral.

Approach:

The patient was seen immediately by a pulmonologist at the Women's Lung Health Program. In collaboration with her obstetrician in Maternal-Fetal Medicine, she was begun on a short course of oral corticosteroids. Her respiratory status quickly improved. She also was given a nasal steroid inhaler and nasal saline irrigation for her nasal and sinus congestion, with good effect. Influenza vaccine was administered and ongoing follow-up was provided by her BWH pulmonologist. Proper use of her inhalers was reviewed, and emphasis was placed on careful adherence to her medicines. Symptoms were closely monitored, along with home peak flow measurements and office spirometry. She had one brief hospitalization during her pregnancy, at which time she was admitted to the obstetrical service with pulmonary consultative care. She delivered a healthy baby boy, and mom and son are now doing well.

Women's Lung Health Program



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