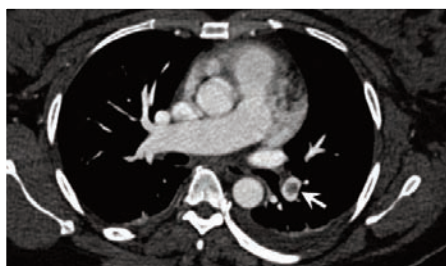
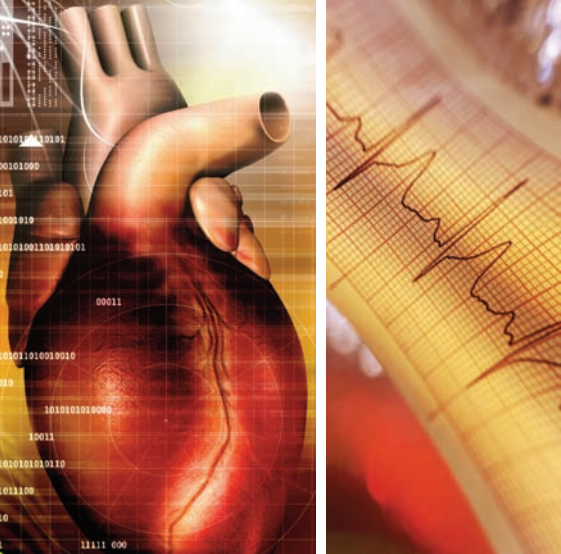




BRIGHAM AND WOMEN'S HOSPITAL

Cardiovascular Center Update



Page 2 **Cardiovascular Disease and Pregnancy Program Provides Expert Evaluation and Care**

The Cardiovascular Disease and Pregnancy Program at Brigham and Women's Hospital is a multidisciplinary program offering expert, coordinated care for women with congenital and other pre-existing heart and vascular disease or cardiovascular conditions arising during pregnancy.



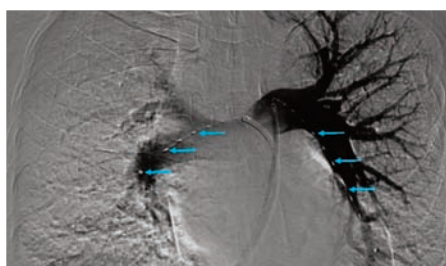
Page 4 **New Center Delivers Diagnosis for Unexplained Dyspnea**

Comprised of a team of specialists in pulmonary medicine, cardiovascular medicine, neurology, and cardiovascular imaging, the Dyspnea Center at Brigham and Women's Hospital provides innovative evaluation, including Advanced Cardiopulmonary Exercise Testing, to determine the cause of dyspnea.



Page 5 **VAD Program Offers Trial of New Total Artificial Heart Driver**

The Ventricular Assist Device (VAD) Program within the Carl J. and Ruth Shapiro Cardiovascular Center is the first and only program in New England to participate in a new study of a portable driver that enables total artificial heart (TAH) patients to return home while awaiting heart transplantation.



Page 6 **Pioneering Novel Approaches to the Prevention, Diagnosis, Treatment, and Research of Venous Thromboembolism**

Specialists in the Venous Thromboembolism (VTE) Research Group at Brigham and Women's Hospital (BWH) are advancing the prevention, treatment, research, and understanding of pulmonary embolism (PE) and deep vein thrombosis (DVT).



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Cardiovascular Disease and Pregnancy Program Provides Expert Evaluation and Care

Directed by maternal-fetal medicine specialist Katherine Economy, MD, and cardiologists Reena Pande, MD, and Anne Marie Valente, MD, the Cardiovascular Disease and Pregnancy Program at Brigham and Women's Hospital is a multidisciplinary program offering expert, coordinated care for women with congenital and other pre-existing heart and vascular disease or cardiovascular conditions arising during pregnancy.

With vast experience in managing cardiovascular issues in pregnancy, Program specialists collaborate to develop a detailed and personalized care plan for each patient – beginning before conception and continuing through pregnancy, labor and delivery, and the post-partum period. A comprehensive assessment of each patient's condition and symptoms is performed with advanced cardiovascular imaging techniques that are safe for use during pregnancy. Necessary adjustments are made to medications early in pregnancy or prior to pregnancy, if the patient is seen before conception.

"Each patient's care plan outlines her individual issues and encompasses anesthesiology and many other disciplines," said Dr. Economy.

Pre-pregnancy Evaluation and Intervention

Whenever possible, cardiovascular issues are addressed prior to pregnancy, including coordinating care with cardiac surgeons, interventional cardiologists, and electrophysiologists, in order to manage existing cardiovascular conditions

Indications for Referral

The Cardiovascular Disease and Pregnancy Program offers expert, coordinated care for women with:

- Congenital heart disease or other pre-existing cardiovascular conditions;
- Cardiovascular disease and related issues arising during pregnancy.

safely during pregnancy. For women with congenital heart disease or other pre-existing cardiovascular conditions who are considering pregnancy, Program specialists communicate risks of pregnancy, as well as steps that should be taken prior to pregnancy. For example, recommendations may include an improvement in fitness level prior to pregnancy to help in managing the changes in hemodynamics that occur during pregnancy.

Collaboration with BACH

Program specialists also work closely with the Boston Adult Congenital Heart (BACH) Service, a program jointly offered by Brigham and Women's Hospital and Children's Hospital Boston for young adult patients with congenital heart disease. Patients who are followed in the BACH program are provided with seamless care during pregnancy by specialists in the Cardiovascular Disease and Pregnancy Program.

Case Study

Congenital Heart Disease and Pregnancy

A 21-year-old woman suffering from fatigue and cyanosis was referred to the Boston Adult Congenital Heart (BACH) Service. Cardiac evaluation determined she had tetralogy of Fallot (TOF) with pulmonary artery atresia. Over the next four years, she underwent a series of staged imaging, catheterizations, functional testing, and surgical procedures to establish effective and controlled pulmonary blood flow, and alleviate intracardiac shunting. She experienced a great increase in exercise tolerance, with resolution of her cyanosis. After counsel, she became pregnant and remained under the care of both cardiologists and high-risk maternal fetal medicine specialists in the BWH Cardiovascular Disease and Pregnancy Program. At 39 weeks gestation, labor was induced, and she underwent successful vaginal delivery of a healthy baby girl.

This image shows a maximal intensity projection of the cardiac magnetic angiogram demonstrating preoperative anatomy in which the lungs received blood flow exclusively from collaterals from the descending aorta (arrows). Deoxygenated blood reaches the systemic arterial circulation directly from the right ventricle to the left ventricle, via an unrepaired ventricular septal defect, leading to systemic arterial cyanosis. The patient underwent staged surgical procedures with ultimate incorporation ("unifocalization") of the aorto-pulmonary arterial collaterals to an aorto-pulmonary shunt – designed to create an interconnected series of pulmonary arterial branches with controlled flow that could later be attached directly to a central pulmonary artery. Subsequent surgery led to takedown of the shunt and placement of a homograft from the right ventricle to these "unifocalized" segments, and closure of the ventricular septal defect – completing an effective pulmonary arterial tree connected to the right ventricle, free of intracardiac shunting.



“The collaboration between the Cardiovascular Disease and Pregnancy Program and the Boston Adult Congenital Heart Service provides patients with a consistent team of providers, who often have cared for them from childhood through early adulthood and into pregnancy,” said Dr. Valente, who also is Director of Outpatient Services for BACH.

Program specialists also address other cardiovascular issues that may arise during pregnancy, including systemic hypertension, pulmonary embolism, deep vein thrombosis, and other conditions, using a multidisciplinary approach to care.

“We work together in order to quickly and safely respond to cardiovascular changes and conditions that may occur during pregnancy,” said Dr. Pande. “These include deep vein thrombosis, pulmonary embolism, cardiac arrhythmias, and a variety of other issues.”



Katherine Economy, MD
Co-director, Cardiovascular Disease and Pregnancy Program,
Maternal-Fetal Medicine Specialist,
Division of Maternal Fetal Medicine,
Brigham and Women’s Hospital



Reena Pande, MD
Co-director, Cardiovascular Disease and Pregnancy Program,
Cardiologist and Vascular Medicine Specialist,
Division of Cardiovascular Medicine,
Brigham and Women’s Hospital

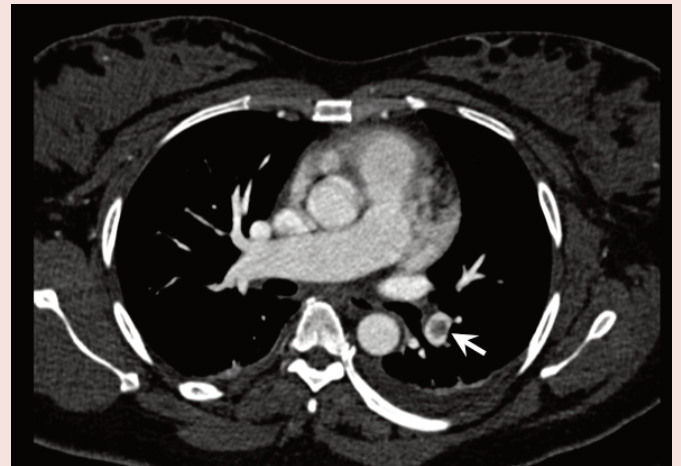


Anne Marie Valente, MD
Co-director, Cardiovascular Disease and Pregnancy Program,
Cardiologist and Adult Congenital Heart Disease Specialist,
Division of Cardiovascular Medicine,
Brigham and Women’s Hospital;
Director, Outpatient Services,
Boston Adult Congenital Heart (BACH) Service,
Brigham and Women’s Hospital and Children’s Hospital Boston

Case Study

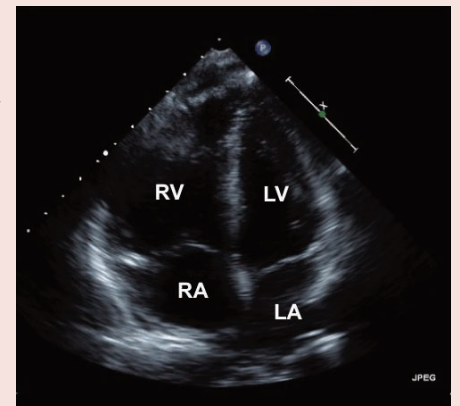
Pulmonary Embolism Developing after Cesarean Section

A 45-year-old otherwise healthy woman underwent a scheduled cesarean section complicated by vaginal bleeding. On the first post-partum day, she developed tachycardia, hypoxia, and shortness of breath. A CT scan of the chest was performed and identified a filling defect in the distal left main pulmonary artery with extension into the lobar branches – consistent with a pulmonary embolism. An echocardiogram revealed right ventricular enlargement and hypokinesis. She was evaluated by a cardiovascular medicine specialist in collaboration with her high-risk maternal fetal medicine specialist in the BWH Cardiovascular Disease and Pregnancy Program. She was safely initiated on unfractionated heparin for anticoagulation. She was ultimately transitioned to Coumadin, which was continued for a six-month treatment period without complication. She was seen in the Watkins Cardiovascular Clinic at one month and six months after discharge and was doing very well without further clinical symptoms.



Multi-detector CT of the chest was performed with administration of intravenous contrast. A filling defect consistent with a pulmonary embolism is seen in a branch of the left main pulmonary artery (*arrow*). Further extension was noted into the lobar segmental and subsegmental branches within the left upper and left lower lobes.

Two-dimensional echocardiography demonstrated significant right ventricular enlargement and hypokinesis (RV = right ventricle, LV = left ventricle, RA = right atrium, LA = left atrium).



Information and Referrals

For more information, or to refer a patient, please contact our Referral Coordinator at (617) 732-9894 or email bwhreferrals@partners.org.

New Center Delivers Diagnosis for Unexplained Dyspnea

Led by pulmonologist Aaron B. Waxman, MD, PhD, and cardiologist Daniel E. Forman, MD, the new Dyspnea Center at Brigham and Women's Hospital provides innovative evaluation to determine the cause of dyspnea – a common symptom that often eludes definitive diagnosis.

Comprised of a team of specialists in pulmonary medicine, cardiovascular medicine, neurology, and cardiovascular imaging, the Center greatly reduces work-up time and speeds diagnosis for patients with unexplained dyspnea. The team is among few in the nation to offer highly specialized cardiopulmonary exercise testing designed to pinpoint the source of dyspnea and exercise limitation. Advanced Cardiopulmonary Exercise Testing at Brigham and Women's Hospital is performed by right heart catheterization and placement of a radial arterial line to evaluate heart and lung hemodynamics and assess how the patient is utilizing oxygen.

"The information gleaned from this testing far outweighs other available technology," said Dr. Waxman. "In nearly all cases, we are able to identify the underlying cause of dyspnea and contributing factors."

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Indications for Referral

Patients with unexplained dyspnea may be referred to the Dyspnea Center for:

- Unexplained exertional symptoms with normal or inconclusive EKG, Echo, PFTs, and imaging;
- Symptoms out of proportion with resting abnormalities on Echo, PFTs, and imaging;
- No improvement with "standard therapy" for suspected diagnosis, such as asthma, COPD, or CHF;
- Mixed co-morbidities that contribute to dyspnea and determination of appropriate treatment;
- Operative risk stratification;
- Pre-transplant evaluation;
- Evaluation of response to treatment;
- Fitness assessment and response to rehabilitation or training.



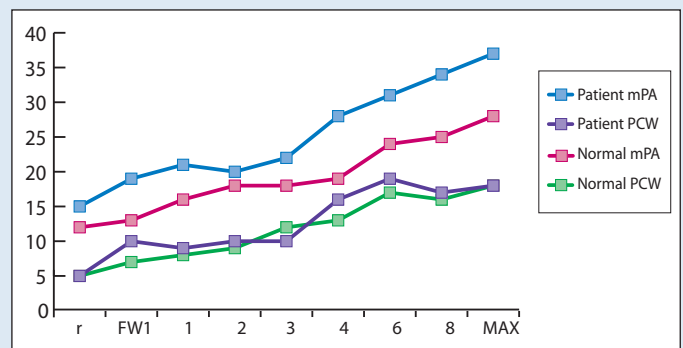
Aaron B. Waxman, MD, PhD
Director, Dyspnea Center,
Pulmonologist, Brigham and Women's Hospital



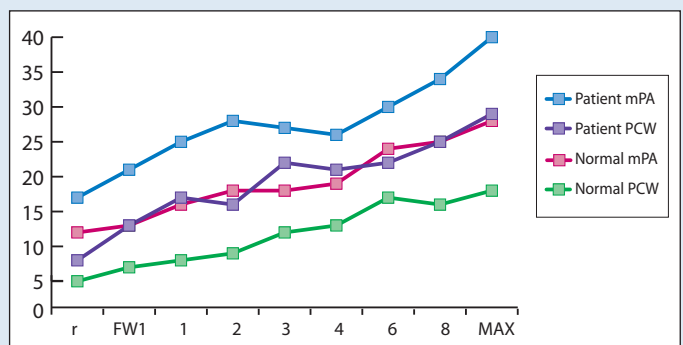
Daniel E. Forman, MD
Co-director, Dyspnea Center,
Cardiologist, Brigham and Women's Hospital

Case Studies: Determining Cause of Unexplained Dyspnea

A 38-year-old woman was evaluated for dyspnea and tachycardia with exertion. Her physical exam, echocardiogram, a pulmonary embolism protocol computed tomogram of the chest, pulmonary function testing, and the diffusing capacity for carbon monoxide (DLCO) were all normal. Standard non-invasive cardiopulmonary exercise testing showed early anaerobic threshold (AT) and low VO₂max (oxygen uptake at peak exercise) of 77 percent. Invasive or Advanced Cardiopulmonary Exercise Testing included cycling for 8.75 minutes to 131.3 watts. VO₂max was 78 percent of predicted, heart rate response was 110 percent of predicted, and an early AT was evident. Findings (see graph below) were consistent with exercise-induced pulmonary arterial hypertension (eiPAH). The patient was started on Bonsentan. Within one month, her symptoms were markedly improved.



A 59-year-old woman presented with progressive dyspnea on exertion. Echocardiogram and computed tomogram of the chest were both normal. Mild restriction on pulmonary function testing and normal diffusing capacity for carbon monoxide (DLCO) were found. Advanced Cardiopulmonary Exercise Testing included cycling for 9.3 minutes to 93 watts. The exercise test was stopped because of leg fatigue. The oxygen uptake at peak exercise (VO₂max) was 82 percent of predicted with normal anaerobic threshold (AT) and normal cardiac output. Hemodynamics (see graph below) were consistent with heart failure with preserved ejection fraction (HFpEF) or diastolic dysfunction. The patient was started on Tadalafil with significant improvement in dyspnea and near resolution of symptoms after a few weeks.



VAD Program Offers Trial of New Total Artificial Heart Driver

The Ventricular Assist Device (VAD) Program within the Carl J. and Ruth Shapiro Cardiovascular Center at Brigham and Women's Hospital is the first and only program in New England to participate in a new study of a portable driver (SynCardia Freedom® Driver) that enables total artificial heart (TAH) patients to return home while awaiting heart transplantation. Program specialists are currently recruiting patients for this trial and will soon perform the first TAH implantation in the region.

Addressing Long Organ Wait Times

The FDA-approved Investigational Device Exemption (IDE) clinical study is evaluating a 13.5-pound portable driver that allows patients who meet stability criteria to begin a phased discharge from the hospital following successful TAH implantation. Previously, patients who underwent TAH implantation have remained connected to a 418-pound driver ("Big Blue") in the hospital until a suitable donor heart became available.

"As wait times for heart transplantation average between six and 12 months in the New England region, the total artificial heart has not been an ideal option for our patients with biventricular heart failure," said Michael M. Givertz, MD, Medical Director of the VAD Program. "We are now able to offer this technology without confining patients to the hospital for long periods of time."

Outcome studies of patients who have received in-hospital TAH support while awaiting transplantation showed a 79 percent bridge-to-transplantation survival rate (*N Engl J Med* 2004; 351:859-67). The total artificial heart offers several advantages when compared with biventricular assist devices. In addition to constituting one device over two pumps, the new portable TAH driver is lighter than equipment supporting biventricular assist devices, and the risk of TAH mechanical failure is extremely low.

Pioneering New Advances

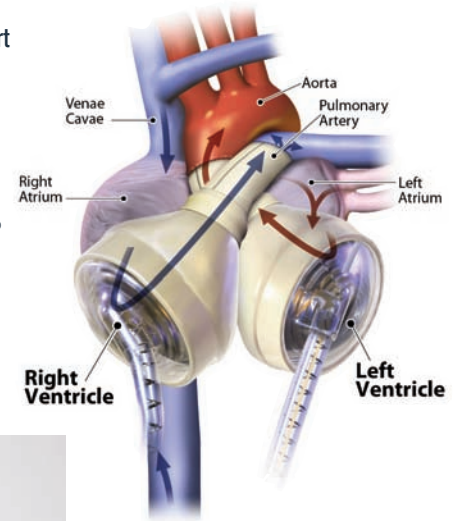
The VAD Program provides a wide range of options for patients with advanced heart disease and has led the region's investigation of many new circulatory assist devices, including the following trials:

- HeartMate II® as destination therapy;
- TandemHeart® Percutaneous VAD;
- Abiomed's Impella® 2.5 for high-risk PCI.

Access and Information

To refer a patient for consideration of a ventricular assist device, heart transplantation, or other advanced heart failure therapies, please call the Advanced Heart Disease Program at (617) 732-7141.

The SynCardia Total Artificial Heart (right) is FDA approved as a bridge-to-transplantation device. Brigham and Women's Hospital specialists are the first in New England to offer a trial evaluating the SynCardia Freedom® Driver (below), which enables TAH patients to return home while awaiting a suitable donor heart, and will soon perform the first TAH implantation in the region.



Images courtesy of SynCardia.com

Specialists at Brigham and Women's Hospital also performed the first heart transplantation in New England and recently completed their 600th heart transplantation – the highest volume in the region.

"We strive to provide the most advanced treatments and the most optimal therapies for each patient, with the goal of returning patients home and to their communities as quickly as possible," said Gregory S. Couper, MD, Surgical Director of the VAD Program.

Successful Discharge Home

The VAD Program enables approximately 95 percent of patients to return home following VAD implantation, including three out of four patients who receive a biventricular assist device. Program specialists place extensive emphasis on patient, family, and

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Gregory S. Couper, MD
Surgical Director,
Ventricular Assist Device Program



Michael M. Givertz, MD
Medical Director,
Ventricular Assist Device Program

Pioneering Novel Approaches to the Prevention, Diagnosis, Treatment, and Research of Venous Thromboembolism

Specialists in the Venous Thromboembolism (VTE) Research Group at Brigham and Women's Hospital (BWH) are advancing the prevention, treatment, research, and understanding of pulmonary embolism (PE) and deep vein thrombosis (DVT).

"Pulmonary embolism is the most preventable cause of death among hospitalized patients and accounts for up to 180,000 deaths per year in the United States," said Samuel Z. Goldhaber, MD, Director, VTE Research Group. "Our goal is to prevent PE and DVT, as well as to improve outcomes among patients who develop these conditions."

Computerized Physician Alerts Prevent VTE

The VTE Research Group and BWH Information Technologies have been at the forefront of developing computerized alerts for physicians with hospitalized patients who are at high risk for developing venous thromboembolism. In a 2,500-patient randomized clinical trial led by Dr. Goldhaber and published in *The New England Journal of Medicine* (*N Engl J Med* 2005;352: 969-977.), researchers at BWH found that computer alerts that encouraged prophylaxis use among high-risk hospitalized patients resulted in a 41 percent decrease in symptomatic PE and DVT. A subsequent and more sophisticated version of this alert system, designed to better ensure implementation of prophylaxis against DVT and PE in high-risk patients, has shown even greater effectiveness (*Thromb Haemost* 2010; 103: 312-317).

Groundbreaking Clinical Trials Shape Care

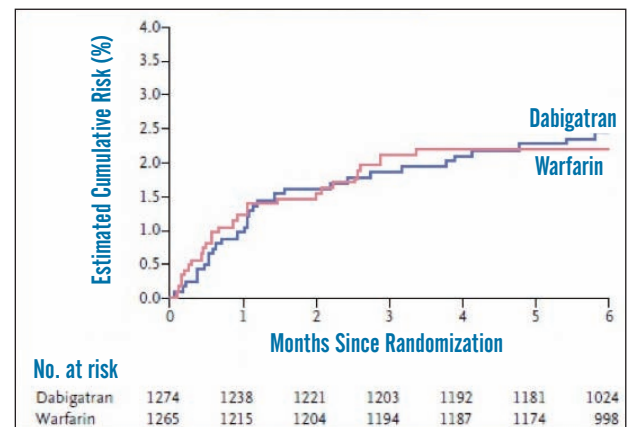
BWH is a primary referral center in New England for patients with complicated PE and DVT and is currently participating in the ATTRACT (The Acute Venous Thrombosis: Thrombus Removal with Adjunctive Catheter-directed Thrombolysis) trial. This major NIH-sponsored, multicenter national trial for large DVT randomizes patients for either catheter intervention or usual therapy and then follows these patients for several years to determine which patients are at risk for post-thrombotic syndrome. Dr. Goldhaber is the Chair of the Steering Committee for this trial.

Having directed multicenter trials resulting in the FDA approval of tPA for PE, Dr. Goldhaber is now active in national and international guideline committees to educate clinicians about the benefits and risks of the use tPA for PE. For patients who are not candidates for tPA, BWH cardiac surgeons have led the use of pulmonary embolectomy to treat PE – with a 95 percent survival rate.

Dr. Goldhaber was the senior author of a recent trial that tested a novel oral anticoagulant medication, dabigatran, compared with warfarin in the treatment of acute venous thromboembolism (*N Engl J Med* 2009; 361:2342-2352.). The study found that, for the treatment of acute venous thromboembolism, a fixed dose of dabigatran is as effective as warfarin, has a safety profile that is similar to that of warfarin, and does not require laboratory monitoring. (see graph)

Through the implementation of computerized decision support protocols, specialists at BWH also are reducing the use of chest CT scans for PE diagnosis, thereby limiting radiation exposure and risks of renal failure and allergic reactions caused by contrast agents.

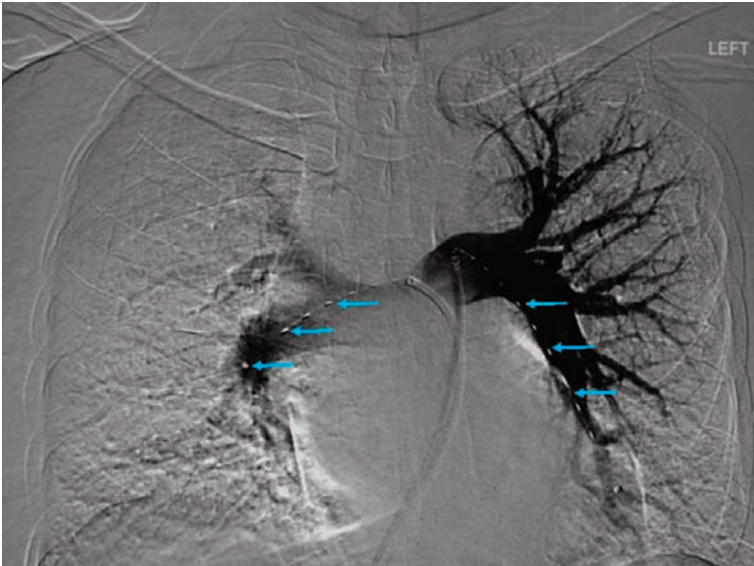
Risk of Recurrent VTE/Death



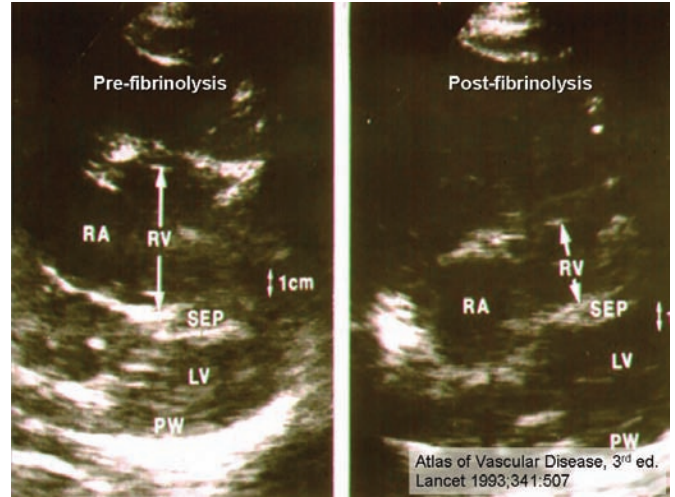
(NEJM 2009; 361: 2342-2352)

Genetics and Epidemiology in VTE

Researchers at BWH also have made significant genetic and epidemiologic discoveries in PE. Paul Ridker, MD, MPH, Director, Center for Cardiovascular Disease Prevention, has led a large randomized trial demonstrating the effectiveness of statin therapy in preventing venous thromboembolism in apparently healthy adults with elevated CRP levels. (*N Engl J Med* 2009; 360:1851-1861). The trial, called JUPITER, randomly assigned 17,802 apparently healthy men and women with both low-density lipoprotein (LDL) cholesterol levels of less than 130 mg per deciliter and high-sensitivity C-reactive protein levels of 2.0 mg per liter or higher to receive rosuvastatin, 20 mg per day, or placebo. Rosuvastatin significantly reduced the occurrence of symptomatic venous thromboembolism by more than 40 percent.



Pulmonary angiography demonstrating successful placement of the EkoSonic Endovascular System catheters in the right and left main pulmonary arteries. Regularly spaced low-power ultrasound transducers (*arrows*) accelerate thrombus dissolution and lower the risk of bleeding by reducing the dose of fibrinolytic drug required.



Surface echocardiography demonstrating marked right ventricular (RV) enlargement relative to the left ventricle (LV) in a patient with PE (*left*). After systemic fibrinolysis, RV chamber size has normalized (*right*).

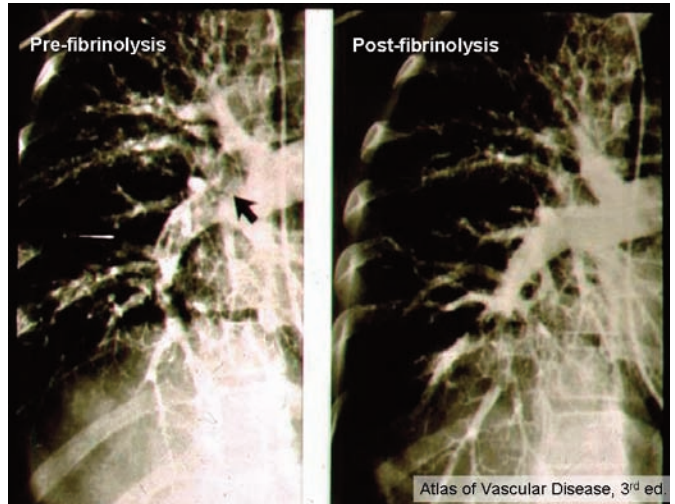
Specialists in the VTE Research Group also established the North American Thrombosis Forum (NATF) – a non-profit organization dedicated to saving lives through thrombosis prevention and education. Members of both BWH and the NATF have worked closely with the Surgeon General’s office to communicate the importance of prevention of PE and DVT and to promote patient advocacy. A long-standing monthly pulmonary embolism support group led by Dr. Goldhaber and his nurse, Ruth Morrison, RN, BSN, addresses the emotional and psychological ramifications of PE.



Samuel Z. Goldhaber, MD
Director, VTE Research Group



Paul Ridker, MD
Director, Center for Cardiovascular Disease Prevention



Pulmonary angiography demonstrating a large PE in the right main pulmonary artery (*left*) before systemic fibrinolysis. After fibrinolysis, there has been marked dissolution of the thrombus (*right*).

Information and Referrals

For more information, or to refer a patient, please contact our Referral Coordinator at (617) 732-9894 or email bwhreferrals@partners.org.

New Center Delivers Diagnosis for Unexplained Dyspnea

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Other specialists in the Center include pulmonologists Barbara A. Cockrill, MD, Bartolome R. Celli, MD, Miguel Divo, MD, and Anne L. Fuhlbrigge, MD, neurologist Thomas I. Cochrane, MD, Marcelo F. Di Carli, MD, Chief, Nuclear Medicine and Molecular Imaging, and Director, Cardiovascular Noninvasive Imaging Program, and Victor H. Gerbaudo, PhD, Senior Administrative Director, Cardiovascular Noninvasive Imaging Program.

Once a diagnosis is made, results are reported back to the patient's referring physician. The team also makes recommendations for treatment and referral to other specialists, if needed or desired. Experts in a wide range of disciplines at Brigham and Women's Hospital are available to assist in the treatment of patients with dyspnea related to pulmonary, cardiovascular, neuromuscular, and other conditions.

Information and Referrals

For more information, or to refer a patient, please contact our Referral Coordinators at (617) 732-9894 or email bwhreferrals@partners.org.

VAD Program Offers Trial of New Total Artificial Heart Driver

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caregiver education regarding VAD equipment and overall patient care, as well as post-operative rehabilitation. A VAD support group has allowed patients and family members to share their experiences about living with mechanical circulatory support.

Indications for Referral

Patients with advanced biventricular heart failure who are candidates for cardiac transplantation may be eligible for the SynCardia Total Artificial Heart. Once considered stable following implantation, patients may begin a phased discharge from the hospital using the SynCardia Freedom® Driver.

Cardiovascular Center Access Information



Watkins Cardiovascular Clinic

The one-stop Watkins Cardiovascular Clinic is a comprehensive outpatient clinic that provides centralized scheduling, integrated clinics, and access to multidisciplinary cardiovascular practices. To refer a patient to the Clinic, call (857) 307-4000.

Cardiovascular Access Managers

Our Cardiovascular Access Managers, Lisa Downey, RN, BSN, and Brian Laneau, RN, BSN, facilitate patient transfers and consultations to the Cardiovascular Center. They work closely with the MDConnect patient transfer service, cardiovascular leadership, and referring physicians and hospitals to provide assistance for consultations and direct referrals to the Cardiovascular Center. The Access Managers are available Monday through Friday, 7 a.m. to 5 p.m. at (617) 543-4170 (mobile) or through the page operator at (617) 732-5700, ID #12437. Evening and weekend calls go to MDConnect, our inpatient transfer service.

Physician Liaison

Physician Liaison Ellen Steward provides direct assistance with patient referrals and consultations with our specialists. Ellen is available to meet with you in person and can be reached at (617) 732-9598, esteward@partners.org, or pager (617) 732-5700, ID #36031.