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Heart-Kidney Combined Transplant in a Pediatric Patient at Mayo Clinic



Richard C. Daly, MD, Jonathan N. Johnson, MD, and Carl H. Cramer, MD

The first pediatric heart transplant at Mayo Clinic was performed in 1991. More than 400 heart transplants have been performed at Mayo Clinic in Rochester; of these, more than 40 have been in pediatric patients (younger than 18 years), and 30 more have been performed in adult patients with congenital heart disease. Mayo Clinic pediatric patient survival after transplant exceeds the UNOS/SRTR expected average survival at 1 month and 1 year; 1-year survival for patients who received transplants at Mayo Clinic since 2009 is 100%. Multiorgan transplants in adult patients with congenital heart disease, including heart-kidney, heart-liver, and heart-lung combined transplants, have been performed with excellent success at Mayo Clinic.

A Case of Multiorgan Transplant

The first pediatric combined heart-kidney transplant at Mayo Clinic was performed earlier

this year in a 14-year-old boy. After diagnosis of restrictive cardiomyopathy, he had undergone an isolated heart transplant in 2002. He did very well initially after the transplant, even playing on his school basketball team. However, in the fall of 2011, he began to have episodes of lightheadedness and fainting while running down the basketball court. A treadmill exercise stress test was able to reproduce his symptoms of dizziness at maximal exercise, with concurrent ST-segment elevation.

Coronary angiography was performed (Figure 1) and demonstrated severe coronary vasculopathy. His left anterior descending coronary artery (LAD) was 90% obstructed by a single discrete lesion. The left main coronary artery and left circumflex coronary artery showed



Figure 1. Left coronary artery angiogram. The arrow indicates the prominent narrowing of the proximal left anterior descending coronary artery.

Pediatric Nephrology
Mayo Clinic in Rochester,
Minnesota

Carl H. Cramer II, MD
James M. Gloor, MD
Marie C. Hogan, MD, PhD
Dawn S. Milliner, MD

Pediatric Cardiology
Mayo Clinic in Rochester,
Minnesota

Frank Cetta, MD, Chair
Michael J. Ackerman, MD, PhD
Samuel J. Asirvatham, MD
Allison K. Cabalka, MD
Bryan C. Cannon, MD
David J. Driscoll, MD
Ben Eidem, MD
Donald J. Hagler, MD
Jonathan N. Johnson, MD
Patrick W. O'Leary, MD
Timothy M. Olson, MD

Cardiovascular Surgery
Mayo Clinic in Rochester,
Minnesota

Joseph A. Dearani, MD, Chair
Harold M. Burkhart, MD
Richard C. Daly, MD
Kevin L. Greason, MD
Lyle D. Joyce, MD, PhD
Alberto Pochettino, MD
Soon J. Park, MD
Hartzell V. Schaff, MD
John M. Stulak, MD
Rakesh M. Suri, MD, DPhil

30% lesions. His right coronary artery was 50% obstructed in several locations. Additionally, diffuse atherosclerotic disease was seen distally. A drug-eluting stent was placed successfully across the area of stenosis in the LAD (Figure 2). An implantable cardioverter-defibrillator was also placed because of his potential for ischemia-induced arrhythmia. His renal function was abnormal but not yet to the point of needing consideration for kidney transplant. The patient was able to return home and resume normal activities. However, based on our understanding of the natural history of patients with severe coronary lesions after transplant, the patient was listed for a second heart transplant.

Three months after his initial stent placement, he returned for repeat coronary angiography. This angiogram revealed a new site of discrete stenosis just distal to the previous stent placement, despite treatment with aspirin, clopidogrel, and pravastatin. The stent itself also had evidence of in-stent stenosis (Figure 3). The patient underwent repeat stenting of the narrowed area, again with an excellent result.

During these follow-up evaluations, it was noted that his renal dysfunction had worsened. He was seen by our pediatric nephrology transplant colleagues; his chronic kidney disease was secondary to his 9 years of exposure to calcineurin-inhibiting medications to prevent rejection of his initial heart allograft. The decision was made to list him for combined heart-kidney transplant on the basis of his impaired renal function and severe recurrent cardiac allograft vasculopathy.

Three weeks after he was listed for the combined transplant, a donor became available, and he successfully underwent a combined heart-kidney transplant. His postoperative

course was without complications, and he was discharged after only 7 days in the hospital. He has had no evidence of rejection of either organ 4 months after transplant. The transplant team has devised a long-term plan for the patient that will include the use of mTOR-inhibiting medications such as sirolimus to reduce the risk of recurrent coronary vasculopathy in the new heart and the amount of nephrotoxic medication required for antirejection therapy.

Discussion

This patient exemplifies the increasing complexity of patients considered for organ transplants. As more pediatric patients are undergoing cardiac transplant, the number of individuals who “outlive” their transplant is increasing. Furthermore, a notable segment of these pediatric patients have comorbid conditions that contribute to additional system failure. In this patient, renal failure developed as a result of drugs required to control rejection of his original heart transplant. These complex patients are well served by the multidisciplinary approach employed in the Mayo Clinic Model of Care. In this patient, pediatric cardiologists, adult cardiologists, pediatric nephrologists, and transplant surgeons worked together to provide the best care possible for the patient. And the patient has already started asking when he can play basketball again.

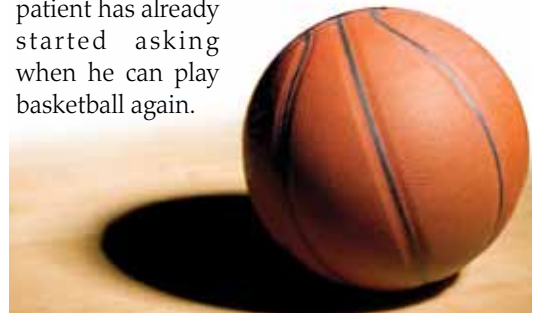


Figure 2. A drug-eluting stent was placed across the area of narrowing, with marked improvement in the coronary artery diameter (arrow).

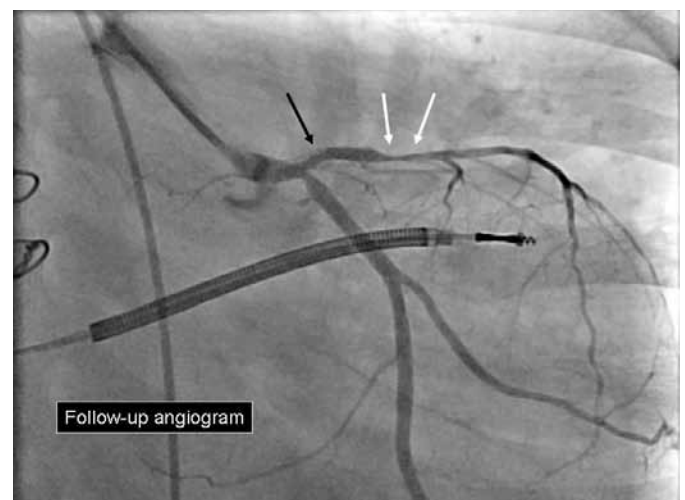


Figure 3. Three-month follow-up angiogram. Note the prominent narrowing of the left anterior descending coronary artery both at the site of the original stent placement (in-stent stenosis, black arrow) as well as distal to that stent (white arrows).

RECOGNITION



Samuel J. Asirvatham, MD, a cardiologist at Mayo Clinic in Rochester, received the Outstanding Teacher Award in February 2012 at the International Dead Sea Symposium on Cardiac Arrhythmias and Device Therapy in Jerusalem, Israel.



Panithaya Chareonthaitawee, MD, a member of the Division of Cardiovascular Diseases at Mayo Clinic in Rochester, has been named Teacher of the Year by residents in the internal medicine training program. She is one of only 6 award recipients at Mayo Clinic in Rochester this year.



Douglas L. Packer, MD, a cardiologist and director of electrophysiology at Mayo Clinic in Rochester, received the Outstanding Achievement Award at the European Cardiac Arrhythmia Society in Munich, Germany, for contributions to the field of cardiac arrhythmia.



Crystal R. Bonnichsen, MD, a trainee in the cardiovascular diseases training program at Mayo Clinic in Rochester has received the Outstanding Achievement Award (Clinical). Dr Bonnichsen has completed her training and has joined the staff of the Division of Cardiovascular Diseases at Mayo Clinic in Rochester.



Thais D. Coutinho, MD, has received the William H. J. Summerskill Award for Outstanding Achievement in Research by a Trainee in a Sub-specialty Clinical Program. This very competitive award was established in 1978 in honor of Dr Summerskill and recognizes subspecialty fellows who have demonstrated excellence in research and have made substantial contributions to the field. Dr Coutinho is a fellow in the cardiovascular disease training program at Mayo Clinic in Rochester.



Andrew D. Calvin, MD, has been named a recipient of the prestigious and very competitive Scott Grundy Fellowship Award for Excellence in Metabolism Research. The award was presented at the Epidemiology and Prevention/Nutrition, Physical Activity, and Metabolism 2012 Scientific Sessions in San Diego, California. This award is named for Dr Scott Grundy, a distinguished leader in the metabolic determinants of atherosclerosis, and is in recognition of Dr Calvin's study on sleep deprivation and its effects on energy intake and expenditure.



Patricia A. Pellikka, MD, has been elected president of the American Society of Echocardiography. Dr Pellikka is a member of the Division of Cardiovascular Diseases and director of the echocardiography laboratory at Mayo Clinic in Rochester.



Jae K. Oh, MD, cardiologist at Mayo Clinic in Rochester, has been elected president of the Asian Pacific Association of Echocardiography. Dr Oh has led collaborative imaging efforts with Samsung Medical Center in Seoul, Korea.

2012 Update on Transcatheter Aortic Valve Insertion

Cardiovascular Surgery Mayo Clinic in Rochester, Minnesota

Joseph A. Dearani, MD, Chair

Harold M. Burkhart, MD
Richard C. Daly, MD
Kevin L. Greason, MD
Lyle D. Joyce, MD, PhD
Alberto Pochettino, MD
Soon J. Park, MD
Hartzell V. Schaff, MD
John M. Stulak, MD
Rakesh M. Suri, MD, DPhil

Cardiac Catheterization and Interventional Cardiology Mayo Clinic in Rochester, Minnesota

John F. Bresnahan, MD, Interim Director

Gregory W. Barsness, MD
Malcolm R. Bell, MD
Patricia J. Best, MD
Barry A. Borlaug, MD
John F. Bresnahan, MD
Allison K. Cabalka, MD‡
Charles R. Cagin, DO*
Frank Cetta, MD‡
Robert P. Frantz, MD
Rajiv Gulati, MD, PhD
Donald J. Hagler, MD‡
Joerg Herrmann, MD
David R. Holmes Jr, MD
Andre C. Lapeyre III, MD
Amir Lerman, MD
Verghese Mathew, MD
Arashk Motiei, MD
Rick A. Nishimura, MD
Krishna M. Pamulapati, MD*
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Guy S. Reeder, MD
Charanjit S. Rihal, MD, MBA
Gupreet S. Sandhu, MD, PhD
Mandeep Singh, MD, MPH
Ripudamanjit Singh, MD*
Paul Sorajja, MD
R. Thomas Tilbury, MD
Henry H. Ting, MD

*Mayo Clinic Health System
‡Pediatric Cardiology



Kevin L. Greason, MD, Rakesh M. Suri, MD, DPhil, and Verghese Mathew, MD

The many developments in the past year related to transcatheter aortic valve insertion (TAVI) include publication of 2-year outcome data of the PARTNER trial cohorts and approval by the US Food and Drug Administration (FDA) of the Edwards Sapien prosthetic aortic valve (Edwards Lifesciences, Irvine, California) for inoperable patients. The development of paravalvular aortic valve regurgitation is a new concern that has been identified in patients receiving these valves (Figure).

Importantly, on November 2, 2011, the FDA approved the Sapien valve for patients with senile aortic valve stenosis, but use is restricted to those considered inoperable by conventional standards for severe, symptomatic aortic stenosis. "The FDA approved the valve for all transarterial avenues, and in general, suitable vascular access can be identified in almost all patients," says Rakesh M. Suri, MD, DPhil, a cardiovascular surgeon at Mayo Clinic in Rochester.

In the PARTNER trial, 699 patients in cohort A were randomly assigned to TAVI (348 patients) or standard operative valve replacement (351 patients). Of the TAVI patients, those with inadequate peripheral vascular access had transaortic valve implantation (104 patients). The 2-year survival data of high-risk patients (ie, those who were otherwise operable) in the PARTNER trial, published in the May 3, 2012, issue of *New England Journal of Medicine*, support TAVI as an alternative to surgery in high-risk patients. Mortality from any cause was similar in the TAVI and standard aortic valve replacement groups ($P=.41$). At 2 years, mortality was 34% in the transcatheter group and 35% in the standard surgery group ($P=.78$).



Figure. Transesophageal echocardiographic image demonstrating paravalvular regurgitation (arrow) in a patient who received a transcatheter prosthetic aortic valve.

Encouragingly, the risk of stroke associated with TAVI appears to level off after the initial spike associated with valve insertion. The original PARTNER high-risk TAVI cohort experienced an increased rate of stroke at 30 days compared with patients treated with standard aortic valve insertion (5.5% vs 2.4%; $P=.04$), and this difference persisted at 1 year (8.3% vs 4.3%; $P=.04$). At 2-year follow-up, however, the frequency of all strokes did not differ significantly between the 2 groups ($P=.52$). It appears that the constant hazard of late stroke is unrelated to the mode of valve replacement. Current efforts are directed at reducing the perioperative risk of stroke (ie, with use of embolic protection devices), thereby making the procedure safer. Earlier this year, a procedural stroke incidence of only 2% was reported in the PARTNER 1A transapical continuing access registry.

"Paravalvular regurgitation has emerged as a major concern associated with TAVI," according to Verghese Mathew, MD, an interventional cardiologist at Mayo Clinic in Rochester. The first reports of this procedure acknowledged that approximately 77% of patients had some degree of paravalvular regurgitation at 30 days. Recent data indicate that at 2-year follow-up, paravalvular regurgitation was unchanged in 46% and worse in 22%. Importantly, the presence of paravalvular aortic valve regurgitation was associated with increased late mortality ($P<.001$). The effect of aortic valve regurgitation on mortality was proportional to the severity of the regurgitation, but even mild aortic valve regurgitation was associated with an increased rate of late deaths.

"It is unclear whether paravalvular aortic valve regurgitation causes late mortality or is simply associated with other causative factors," says Kevin L. Greason, MD, a cardiovascular surgeon at Mayo Clinic in Rochester.

There are 3 reasons why patients develop paravalvular aortic valve regurgitation after TAVI: 1) asymmetric or excessive calcification of the aortic valve annulus; 2) improper assessment of the aortic valve annulus size; and/or 3) valve design. Mayo Clinic investigators are evaluating the first 2 causes with 3-dimensional transesophageal echocardiography and multidetector computed tomography. A better understanding of the dynamic, 3-dimensional structure of the aortic valve annulus throughout the cardiac cycle and how it relates to the emergence of paravalvular regurgitation may improve patient selection. "It is likely that not all patients will have the right valve or annulus size to safely undergo transcatheter valve insertion," according to Dr Greason. Technological advances in the current generation of valve prostheses may better address the problem.

As much as the transcatheter technology has enhanced patient care, more important is the creation of the multidisciplinary heart team to deliver the technology. Cardiologists and cardiac surgeons have combined their talents with remarkable results. When patients are evaluated by the team, the best technology, the best access, and the best technique for aortic valve replacement are identified for the individual patient. "One size does not fit all," says Dr Greason.

NEW STAFF



Alberto Pochettino, MD, has joined the Division of Cardiovascular Surgery at Mayo Clinic in Rochester. Dr Pochettino graduated from Northwestern University and did his general surgical residency at SUNY Health Science Center in Brooklyn, New York. He did his cardiac surgery fellowship at University of Pennsylvania Hospital in Philadelphia and subsequently was director of the pulmonary transplant program at the University of Pennsylvania for 15 years. His interests include aortic disease and aortic valve disease, adult congenital heart disease, reoperative cardiac surgery, and heart and lung transplantation.

RECOGNITION



The American Heart Association has recognized the Florida campus of Mayo Clinic as a Fit-Friendly Company for 2012. This marks the second consecutive year that the Florida campus achieved this designation—one of fewer than 20 organizations in the southeastern United States to be so designated.

Revascularization Strategies

The ideal revascularization strategy—percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG)—for many patients remains uncertain, despite prior randomized trials comparing the 2 approaches.

The American College of Cardiology Foundation (ACCF) and the Society of Thoracic Surgeons (STS) developed a partnership, the ACCF and STS Database Collaboration on the Comparative Effectiveness of Revascularization Strategies (ASCERT), to compare outcomes of these 2 approaches. Data from almost 2 million Medicare patients collected between 2004 and 2007 in these 2 databases, with follow-up data from claims records of the Centers for Medicare and Medicaid Services, were analyzed retrospectively. The study, published in the April 19, 2012, issue of *New England Journal of Medicine*, found that in patients older than 65 years undergoing nonemergent revascularization, there was no difference in 1-year mortality between PCI and CABG; however, mortality was lower at 4 years in patients selected for CABG.

“This trial was unique in that it linked clinical and administrative databases to obtain outcomes in a large patient population,” according to Issam D. Moussa, MD, chair of the Division of Cardiovascular Diseases at Mayo Clinic in Florida and one of the study’s authors. The findings of this study, however, were limited by its retrospective nature, physician referral bias, and the inability to adjust for potentially important confounders, such as incomplete revascularization, patient frailty, and surgical turndowns in the PCI group.

The generalizability of findings from retrospective comparative effectiveness studies of CABG vs PCI is contingent on adequate adjustment of confounders and selection bias, a goal that may not be easily achievable. Therefore, prospective, randomized clinical trials are, and will remain, the gold standard in guiding clinical decision making in patients with obstructive coronary artery disease.

Mayo Clinic Study Confirms Stents Are Safe for Patients Allergic to Metal

Mayo Clinic researchers have found that cardiac patients who have skin allergies to metals commonly found in jewelry, such as nickel, are at no higher risk for complications if they receive a stent containing these metal components.

Mayo Clinic cardiologist Rajiv Gulati, MD, DPhil, and colleagues studied a total of 29 patients with a history of skin allergies to stent metal components who subsequently underwent coronary stent implantation. The research team compared clinical outcomes with a matched control group of 250 patients not allergic to metal who received similar stents. In addition to following the study patients’ outcomes in the long term, the team reviewed blood to look for signs of allergic reactions. In the study, published in the April 2012 issue of *Circulation: Cardiac Interventions*, a history of metal allergies was not associated with acute allergic reactions or an increased rate of restenosis.

“Healthiest Family”

D. Eric Steidley, MD, a cardiologist at Mayo Clinic in Arizona, and his family were recently named Arizona’s “healthiest family” by *Arizona Parenting Magazine* and ShapeUp USA, an organization dedicated to preventing childhood obesity and empowering families to lead healthier and more meaningful lives.



New Technology Enables Novel Remote Health Care



Charles J. Bruce, MD
Mayo Clinic in Rochester



Virend Somers, MD, PhD
Mayo Clinic in Rochester



Paul A. Friedman, MD
Mayo Clinic in Rochester

A multidisciplinary team at Mayo Clinic in Rochester, including members of the Division of Cardiovascular Diseases and the Department of Engineering, has been developing remote monitoring technology for the past decade. One of the outcomes of this initiative is the development of the BodyGuardian remote monitoring platform.

The vision has been to develop an integrated, adaptable system for screening, prevention, and management of disease that serves as a “dashboard” of overall health and well-being (much like the sensor system does in a modern car). The team has developed a broad-based remote monitoring system that enables continuous or intermittent physiologic monitoring and detection of abnormalities arising from a range of medical conditions before they lead to clinically significant concerns. The recorded information is fed into algorithms, giving the health care provider the ability to assess the patient, even though the patient may be thousands of miles away. For example, when the patient experiences changes, such as weight gain beyond a threshold amount, the algorithms will prompt the patient and provider to adjust diet and exercise. An increased resting respiratory rate might prompt a medication adjustment.

This physician-directed, patient self-management approach will potentially help maintain wellness by frequent adjustments in evidence-based medical therapy, without the need for the patient to travel to the provider’s office. When the patient has a clinically relevant event, the BodyGuardian communicates wirelessly with a smartphone, provided to the patient. The smartphone inquires about patient symptoms; then event data are sent securely, via the cell phone network and the Internet, to the patient’s caregiver for appropriate intervention, all in real time. The smartphone is the communication hub; it stores data, sends messages and reminders, and provides coaching suggestions. Patients may also enter information.

BodyGuardian potentially avoids the necessity of traditional in-hospital monitoring or surgical implantation of sensors. The invention allows noninvasive on-body monitoring that is prescribed and monitored by health professionals with technology that is designed to be unobtrusive for caregivers and patients. The technology provides valuable real-time feedback to the person wearing the monitor and to the health care team. Watching patients from afar and helping them help themselves with as little medical intervention as possible benefit patients, their family members, and the health care team: a true “personal guardian angel.”

The BodyGuardian represents innovation and collaboration within Mayo Clinic’s integrated clinical and engineering practices, facilitated by US and European industry partners. The device is being evaluated in clinical trials at Mayo Clinic by a multidisciplinary team of internists, cardiologists, behavioral scientists, hardware and software engineers, and industry partners. In these trials, the device is being refined and validated in patients with heart failure and rhythm disorders in post-ICU step-down settings, as well as in elderly subjects living independently in an assisted living environment.



Figure. BodyGuardian device is small and portable, facilitating ease of use and patient compliance.

Mayo Clinic

Cardiovascular Update

Medical Editor:

Margaret A. Lloyd, MD, MBA

Editorial Board:

Charanjit S. Rihal, MD, MBA

Issam Moussa, MD

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Managing Editor:

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Marjorie G. Durhman

Photography:

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Arizona

866-629-6362

Florida

800-634-1417

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800-533-1564

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Ventricular Function in Congenital and Acquired Heart Disease: From Doppler to Deformation—State of the Art in 2012

Oct 5-6, 2012, Rochester, MN

28th Annual Echocardiography in Adult and Pediatric Congenital Heart Disease

Oct 7-10, 2012, Rochester, MN

22nd Annual Cases in Echocardiography, Cardiac CT and MRI

Oct 24-27, 2012, Napa, CA

Southwest Electrophysiology Course: Bridging the Gap Between Specialist and Internist

Oct 25-27, 2012, Phoenix, AZ

Mayo Clinic Satellite Educational Program at AHA 2012

Nov 3-7, 2012, Los Angeles, CA

Coronary Artery Disease: Prevention, Detection, and Treatment

Nov 15-17, 2012, Las Vegas, NV

Echo on Marco Island: Case-Based Approach

Dec 6-9, 2012, Marco Island, FL

The Heart Beat of Cardiology: Practical Application of Echocardiography

Dec 13-15, 2012, Chicago, IL

Case Studies in Structural Heart Disease

Jan 24-27, 2013, Sunny Isles, FL

Arrhythmias and the Heart: A Cardiology Update

Jan 28-Feb 1, 2013, Maui, HI

38th Annual Cardiovascular Conference at Snowbird

Feb 4-7, 2013, Snowbird, UT

Hawaii Heart 2013: Echocardiography and Multimodality Imaging: Case-Based Clinical Decision Making

Feb 4-8, 2013, Kauai, HI

18th Annual Cardiology at Cancun

Feb 25-Mar 1, 2013, Cancun, Mexico

20th Annual Echocardiographic Workshop on 2-D and Doppler Echocardiography at Vail

Mar 11-14, 2013, Vail, CO

Heart Failure Management for NPs, PAs, and Primary Care Providers

Mar 17-19, 2013, San Antonio, TX

Echo Fiesta: An In-Depth Review of Adult Echocardiography for Sonographers and Physicians

Mar 21-24, San Antonio, TX

Echocardiography for the Nation's Capital: Practical Review of Adult Echocardiography for Physicians and Sonographers

Apr 13-15, 2013, Washington, DC

Cardiology in the Capital

Apr 25-27, 2013, Washington, DC

Mayo Echocardiography Review Course for Boards

May 3-7, 2013, Rochester, MN

Basic to Advanced Echocardiography: From the Blue Ridge Mountains of Asheville

May 8-11, 2013, Asheville, NC

Clinical Autonomic Quantitation Workshop

May 17-19, 2013, Rochester, MN

16th Annual International Course on Cardiology and Cardiac Surgery

Aug 5-9, 2013, Vina del Mar, Chile

OTHER EDUCATION OPPORTUNITIES

American Heart Association: Scientific Sessions 2012

Nov 3-7, 2012, Los Angeles, CA

Website: my.americanheart.org

ACC.13: 61st Annual Scientific Session

Mar 9-11, 2013, San Francisco, CA

Website: www.accscientificsession.org

International Society for Heart and Lung Transplantation 33rd Annual Meeting and Scientific Sessions

Apr 24-27, 2013, Montréal, Québec

Website: www.ishlt.org

Heart Rhythm Society 34th Annual Scientific Sessions

May 8-11, 2013, Denver, CO

Website: www.hrsonline.org

Society for Cardiovascular Surgery and Interventions Scientific Sessions

May 8-11, 2013, Orlando, FL

Website: www.scai.org

Heart Failure Congress 2013

May 25-28, 2013, Lisbon, Portugal

Website: www.escardio.org



Visit Mayo Clinic's landing page on theheart.org for the latest cardiology insights—from the bench to the bedside at www.theheart.org/mayoclinic.

MAYO CLINIC | mayoclinic.org

4500 San Pablo Road
Jacksonville, FL 32224

200 First Street SW
Rochester, MN 55905

13400 East Shea Boulevard
Scottsdale, AZ 85259

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