Mortality in the United States due to cardiovascular disease has declined in recent decades, but still more than one in three American adults—80 million people—live with cardiovascular disease in one form or another. It is anticipated that in 2009 Americans will spend more than $475 billion in direct and indirect costs for major cardiovascular disease. The global picture is no better, with nearly one-third of the world’s people dying from cardiovascular diseases—and no projected reduction on the horizon.

Rapid advances in medical technology and treatments hold the promise of reducing death and disability caused by cardiovascular diseases. From the ability to detect heart disease at its earliest stages to a broad and growing range of innovative treatments and devices, the potential exists to extend millions of lives.

Every department within Mount Sinai Heart contributes to this goal, and the Department of Health Evidence and Policy coordinates a broad portfolio of clinical cardiovascular research in collaboration with the Cardiovascular Institute.

Led by Chairman Eric A. Rose, MD, who is also Associate Director of Clinical Outcomes at Mount Sinai Heart, and co-chairs Annetine C. Gelijns, PhD, and Allan Moskowitz, MD, the department is developing evidence on health outcomes, comparative effectiveness, optimum resource allocation, and the reduction of disparities with the InCHOIR (International Center for Health Outcomes and Innovation Research) as its cornerstone. The unit also coordinated the landmark REMATCH (Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure) trial, supported by the National Institutes of Health (NIH), which first proved the survival and quality-of-life benefit of left ventricular assist devices (LVADs) for patients with end-stage heart failure who are not candidates for transplantation.

Dr. Gelijns and Michael Parides, PhD, who leads the department’s biostatistics efforts, are the principal investigators for the multi-center NIH-sponsored Cardiovascular Surgery Clinical Trials Network. The network initiated a broad array of trials focused on surgical management of moderate and severe mitral regurgitation, atrial fibrillation, postoperative infection, and descending aortic dissection. Dr. Moskowitz is the principal investigator of the coordinating center for the NIH-supported ARUBA study (A Randomized Trial of Un-ruptured Brain Arteriovenous Malformations), which is studying whether patients should be managed by intervention or continued observation. Physicians and researchers in Mount Sinai’s Departments of Neurosurgery and Neurology are participating investigators in the trial.

Deborah Ascheim, MD, who leads cardiovascular clinical trials, and Dr. Rose lead NIH-supported trials exploring the role of mesenchymal stem cell implantation in patients receiving LVADs as a bridge to heart transplantation. The research goal is to determine the feasibility of such stem cell implants as an alternative to cardiac allotransplantation. They are also initiating an NIH-supported trial of use of a selective Factor IX antagonist as a new approach to anticoagulation in patients with LVADs. InCHOIR also coordinates multiple industry-sponsored trials of novel second- and third-generation LVADs designed for bridging to transplantation and destination therapy.

Together with advances in biotechnology and policies that support population-level prevention, these and other Mount Sinai Heart initiatives have the potential to substantially reduce the worldwide burden of cardiovascular disease.

VALENTIN FUSTER, MD, PHD
Director, Mount Sinai Heart
FEATURE STORY
4 Ventricular Assist Devices:
Advancing care for patients with heart failure

THIS ISSUE
9 Gene Therapy Could Treat Severe Heart Failure
11 Nurses Reducing the Impact of Heart Failure
13 Diagnosis and Management of Fetal Cardiac Arrhythmias
18 Real-Time 3-Dimensional Intraoperative Transesophageal Echocardiography
20 Clinical Trials Update
21 New Faces
Introducing: Kevin G. Dunsky, Umesh Gidwani, Lynne A. Glasser, Ajith Nair, Timothy Vittorio, Jose M. Wiley, Sujata Chakravarti, Miwa Geiger, James Nielson, Rowan Walsh, and Ageliki G. Vouyaka

CALENDAR OF EVENTS
22 2009 Live Symposium of Complex Coronary and Cardiovascular Cases
Ventricular Assist Devices

ADVANCING CARE FOR PATIENTS WITH HEART FAILURE

by SEAN P. PINNEY, MD

For nearly three decades, heart transplantation has been the treatment of choice for patients suffering from advanced heart failure. Survival in the first year now exceeds 85 percent in most centers, and long-term survival is the norm rather than the exception. In spite of this success, heart transplantation remains limited by a fixed rate of organ donation. It is estimated that 250,000 Americans are living with end-stage heart failure. Approximately 10,000 are currently on a transplant waiting list, but only 2,000 will receive a new heart this year. Viewed from the perspective of the recipient, heart transplantation is a miracle. Viewed from the perspective of supply and demand, heart transplantation is epidemiologically trivial. Ventricular assist devices may help bridge this gap.

Ventricular assist devices (VADs) are miniaturized blood pumps first developed to support the circulation of open-heart surgery patients whose hearts were too weak to wean from cardiopulmonary bypass. In 1964 the National Institutes of Health (NIH) launched an artificial heart program promoting innovation and collaboration among engineers, clinical researchers, and industry to develop mechanical circulatory support devices that would enhance the lives of patients with advanced heart failure.

The early results were the first generation of left ventricular assist devices (LVADs), which received Food and Drug Administration (FDA) approval in the mid-1990s to support patients awaiting transplantation. The past decade has witnessed the development of a new generation of devices that are smaller, more durable, and that hold the promise of standing as an alternative to transplantation.
VENTRICULAR ASSIST DEVICES: A BRIDGE TO TRANSPLANTATION

There are now three generations of VADs. First-generation devices are pulsatile, positive displacement pumps. These are bulky, as they deliver a stroke volume of 60–80 ml. All but one of the FDA-approved devices fall into this category. Examples are the Heartmate XVE (Figure 1), the Thoratec PVAD and IVAD, and the Novocar LVAS.

Second-generation, or axial flow, pumps generate continuous flow by a rotary impeller suspended by contact bearings in the bloodstream. By comparison, these pumps are miniature—about one-fifth the size of first-generation pumps. Only one, the Heartmate II (Figures 2 and 3), is FDA approved for bridging to transplantation. Other investigational second-generation devices include the Jarvik 2000 and Micromed Debakey pumps.

Third-generation VADs also create continuous flow, but they do so by a single rotary impeller that is either magnetically or hydrodynamically suspended. By eliminating the need for contact bearings, these devices could, in theory, last forever and be less likely to lead to thrombus formation. Examples of these investigational devices include the Ventrassist, Heartware® and Duraheart®, which will enter clinical trials at Mount Sinai Heart later this year.

Continuous-flow VADs are now the devices of choice for bridging patients to transplantation. They are small, quiet, and durable. Their drivelines are about the width of a telephone cord, and they are easy to secure and rarely cause infection. In the pivotal FDA bridge-to-transplant trial, 80 percent of recipients with a Heartmate II pump either were alive on support or had received a transplant at six months’ follow-up.1 Similar results were recently reported with the VentraCor Ventrassist®, a third-generation device.

In spite of the advantages of these devices over pulsatile pumps, there are challenges. All continuous-flow VADs require systemic anticoagulation to prevent thrombus formation. Hemolysis is occasionally caused by the helical blades that typically spin at about 10,000 rpm in the Heartmate II (Figure 4) and 2,100 rpm in the Ventrassist®. Higher spin rates produce greater degrees of hemolysis, which in turn increases the chance of thrombus formation, particularly where radial velocity is reduced at the site of contact bearings. Although organ function does not seem negatively affected by the lack of pulsatility, the inability to palpate a pulse or measure blood pressure by sphygmomanometry can make it difficult to monitor a patient’s clinical status.

The small size and durability of these pumps are already contributing to remarkable results. In 2006, surgeons at Mount Sinai Heart reported the first implantation of a Jarvik 2000 device through a median sternotomy without cardiopulmonary bypass (Figure 5).2 The recipient was weaned off mechanical ventilation...
in less than 24 hours and was out of bed on the first postoperative day. This early success has been reinforced by shorter recovery times, a reduction in length of hospital stay, and improved survival rates. Patients occasionally feel so well with these second- and third-generation devices that they forego transplantation entirely. In one well-documented case, a patient survived more than seven years supported by a Jarvik 2000, ultimately dying from a non-cardiac event. Postmortem inspection of the device found minimal bearing wear, suggesting that if damage to the driveline or battery failure can be avoided, newer-generation pumps could reliably run for years.

VENTRICULAR ASSIST DEVICES: DESTINATION THERAPY

Destination therapy with a VAD can extend and improve the quality of life for patients with advanced heart failure. Led by Eric A. Rose, MD, Chairman of the Department of Health Policy at the Mount Sinai Medical Center, the landmark NIH-supported REMATCH (Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure) trial randomized transplant-ineligible patients either to receive the Heartmate XVE or to continue with optimal medical therapy and found the one-year survival with a VAD nearly double that with medical therapy.

In addition, surveys of NYHA functional class and subjective well-being improved with device therapy compared with medical therapy. Although REMATCH is best viewed as proof of principle for destination therapy, critics have pointed out that one-year survival was only 50 percent for VAD recipients and three out of four patients died within two years. Since the results from REMATCH were published, greater familiarity with the device and revised management protocols have improved clinical outcomes. Two-year survival now approaches 50 percent, accompanied by reductions in clinical adverse events and length of hospital stay.

Since REMATCH was published, greater familiarity with the device and revised management protocols have improved clinical outcomes. Two-year survival now approaches 50 percent, accompanied by reductions in clinical adverse events and length of hospital stay. These enhancements should lead to improved outcomes for VAD recipients and reduced costs for health care payers in the years ahead.

For VAD therapy to become the treatment of choice for the majority of patients with advanced heart failure, however, further improvements are required. Providers must know that they are choosing the right pump for a particular patient and installing it at the optimum time. Reduced size and improved durability are likely to make continuous-flow VADs favored devices for destination therapy. Conclusive results from clinical trials are not yet available.

but early termination of the Heartmate II DT trial on the basis of an interim analysis suggests that this continuous-flow VAD will be superior to the Heartmate XVE. The use of a preoperative risk assessment system can sort potential recipients into low-, medium-, high-, and very high-risk categories for post-VAD mortality. Application of this multivariable score allows clinicians to reserve destination therapy for those patients most likely to benefit. For higher-risk patients, an initial period of stabilization and improved nutrition prior to surgery may allow eligibility at a later date, as guided by this risk-stratification scheme.

VENTRICULAR ASSIST DEVICES: THE PROMISE OF RECOVERY

Until recently, the process of left ventricular remodeling was believed to progress inexorably toward a globular, dysfunctional heart prone to mechanical and electrical failure. Medical therapy with ACE inhibitors or β-blockers could temporarily delay remodeling, but it could not reverse it. We now recognize that the volume and pressure unloading afforded by ventricular assist devices can reverse some of the detrimental changes that typically occur in the remodeled left ventricle. One month after VAD implantation, beneficial reductions in LV end-diastolic diameter and mass typically occur. Hypertrophied muscle cells regress toward a normal phenotype, and cardiac mechanics improve, particularly in those patients who are also treated with ACE inhibitors.

Although the net result of these changes is favorable, in most cases they are insufficient to produce enough recovery of function to allow device removal and obviate transplantation. A recent report from England has engendered the hope that recovery may be attainable in more patients than originally thought possible. In combination with an intensive medical regimen including the beta-2 agonist clenbuterol, 11 of 15 patients enrolled were able to safely undergo device removal, and all enjoyed dramatic improvement in quality of life and freedom from heart failure symptoms.
VENTRICULAR ASSIST DEVICES: FUTURE APPLICATIONS

While VADs may allow for reverse remodeling of the left ventricle, they may also provide a stable platform for re-engineering the heart, in parallel with the promise of stem cells to regenerate myocardium. In the future, patients may undergo a series of therapeutic procedures, first receiving a VAD to generate sufficient blood flow to preserve end-organ function, followed by infusion of stem cells to regenerate damaged myocardium. A similar strategy may combine device therapy with gene therapy.

THE MOUNT SINAI EXPERIENCE

As surgical director of the Ventricular Assist Device Program, Anelechi Anyanwu, MD, Associate Professor, Department of Cardiothoracic Surgery, has overseen the implantation of nearly 100 devices in the past three years. Together with cardiologists at Mount Sinai Heart, Dr. Anyanwu has advanced the understanding of the new generations of VADs, participating in clinical trials of the Ventrisassist and Jarvik pumps. Surgeons at Mount Sinai now implant almost 50 VADs annually, with a survival rate for patients with chronic heart failure above 80 percent. Most patients are discharged one to two weeks sooner than typically reported in clinical trials, and quality of life has been high.

In November 2008, Mount Sinai became the first program in Manhattan to receive Joint Commission accreditation for its Ventricular Assist Device Program. This designation is given only to those programs with the multidisciplinary teams and experience needed to ensure optimum outcomes. It is expected that fewer than 60 centers nationwide will secure this designation, which has been required to treat Medicare patients since March. By treating this volume with excellent outcomes, Mount Sinai has become a leader in VAD therapy.

To learn more, visit www.mountsinai.org/pulse/VADS.

> REFERENCES


> ABOUT THE AUTHOR

SEAN P. PINNEY, MD, is Director of the Advanced Heart Failure and Transplantation Program at Mount Sinai Heart and Associate Professor of Medicine.
While progress with conventional treatment modalities continues to reduce heart failure mortality, there remains a need to explore new therapeutic approaches. Heart failure induced by genetic or specific conditions such as coronary artery disease, hypertension, diabetes, infection, or inflammation results in myocardium with a mixture of replacement fibrosis, and dysfunctional and normal myocytes. The normal myocytes that remain are under continuous stress from hormonal and physical stimuli that can induce apoptosis and cell death or render them dysfunctional; preservation of these myocytes is the target of current therapies with neurohormonal blockade.

Future heart failure therapy will be composed of efforts to regenerate myocardium, with the goal of stem cell therapy being the replacement of lost myocytes, and the goal of gene therapy being the recovery of dysfunctional myocytes and preservation of function in disease-free myocytes. Recent advances in understanding the molecular basis of myocardial dysfunction and the evolution of increasingly efficient gene transfer technology has placed some types of cardiovascular pathophysiology within reach of gene-based therapy.

These abnormalities include defects in sarcoplasmic reticulum (SR) function responsible for abnormal intracellular calcium handling (Figure 1). Deficient SR Ca\(^{2+}\) uptake during relaxation has been identified in failing hearts both in humans and in animal models and has been associated with decreased expression and activity of
SR CA\(^{2+}\)-ATPase (SERCA2a). In addition, there are abnormalities at the membrane level involving sodium-calcium exchange, potassium outward currents (K\(_v\) channels), the sodium-potassium \(\text{ATase}\) pump, downregulation and uncoupling of beta receptors and adenyl cyclase, and changes in myofilament activation.

Rectifying these abnormalities has been the target of pharmacological treatments such as digoxin, \(\beta\)-agonists, and phosphodiesterase inhibitors. Unfortunately, these treatments have been associated with significant toxicity. Novel, more specific therapies have been developed that can correct alterations at various levels in the cardiac cell without side effects.

One such treatment currently under investigation is the overexpression of SERCA2a using gene therapy in patients with advanced heart failure. Mount Sinai and 12 other U.S. medical institutions are currently conducting a phase 2 trial, CUPID (Calcium Up-regulation by Percutaneous Administration of Gene Therapy in Cardiac Disease), to determine whether an adenovirus can successfully deliver to failing myocytes a gene encoding for SERCA, a protein pump involved in handling intracellular calcium. In failing hearts, SERCA is downregulated and leads to impaired myocyte contractility.

Phase 1 results showed that patients who received MYDICAR, the genetically targeted enzyme replacement therapy, showed improvement in several critical parameters of heart failure status: symptoms, function, and key biomarkers.

Phase 1 results showed that patients who received MYDICAR, the genetically targeted enzyme replacement therapy, showed improvement in several critical parameters of heart failure status: symptoms, function, and key biomarkers. If successful, CUPID may further the promise of recovery for patients with advanced heart failure.

As we learn more about the mechanisms leading to heart failure and develop resources to specifically correct these abnormalities, we will be able to develop more effective and personalized treatments.

To learn more, visit www.mountsinai.org/pulse/SERCA.

---

ABOUT THE AUTHOR

**ROGER J. HAJJAR, M.D.** is a Professor of Cardiology and Gene and Cell Medicine at the Mount Sinai School of Medicine and Research Director of the Wiener Family Cardiovascular Research Laboratories at Mount Sinai Heart.

The CUPID trial is funded by Celladon Corporation, makers of MYDICAR. Celladon is a privately held biotechnology company that focuses on molecular therapies for the treatment of heart failure. Dr. Hajjar co-founded Celladon in 2004 prior to assuming his position at Mount Sinai, and he is currently a scientific adviser to the company and a shareholder.
Patients with congestive heart failure (CHF) present a complex array of issues, many of which benefit from coordination of care between nurses and physicians. In 2004 Mount Sinai Heart and North General Hospital formed the Alliance for Health Improvement to enhance the health of residents of East and Central Harlem, incorporating sustainable programs of proven effectiveness into the clinical operations at the diagnostic and treatment centers of the two hospitals.

The first such initiative was the CHF program. An initial study of the effect of nurse management on the quality of heart failure care in minority communities randomized 406 adults with systolic dysfunction ejection fraction less than 40 percent at six neighborhood hospitals to receive usual care or an intervention involving nurse management. The nurse’s primary goal was to improve the patients’ ability to manage their cardiac health using evidence-based guidelines to facilitate communication with physicians overseeing the care of these patients.1,2

The Heart Failure Education and Rehabilitation Training program (HEART), unique to Mount Sinai, is based on the success of this nursing intervention. The patients receive the same benefits of the intervention (health education, scale, contact with a nurse, and health monitoring, all free of charge). To date, more than 200 patients have enrolled. The goal remains to reduce hospital admissions, improve function, and encourage self-care.

At an initial office visit, a nurse assesses the patient’s knowledge of his or her illness, readiness to learn, ability to access community and hospital resources, and ability to care for him- or herself. The nurse emphasizes knowledge of the warning signs of decompensated heart failure; the importance of dietary sodium restriction, monitoring body weight daily, modifying activities, and adhering to prescribed medications; and the appropriate steps to take if symptoms of heart failure worsen.

During the follow-up period, patients record detailed dietary information including assessments of sodium intake. Complimentary scales are given to all patients to help them keep track of their weight. Functional status is assessed at entry and during periodically scheduled telephone calls. During phone calls, patients report symptoms and weight, review medications, and discuss issues of concern. A summary of clinical features from the first 163 participants in the HEART program is shown in Table 1.

When a patient requires hospitalization because of an exacerbation of CHF, call frequency is increased after discharge. Patient care issues are reviewed regularly with the cardiologist leading the program, and recommendations are communicated to primary care providers.

| TABLE 1. Summary of data from the Heart Failure Education and Rehabilitation Training program at Mount Sinai Heart |
|---|---|
| **Active Patients (n=163)** | **Number** |
| **Gender** |  |
| Male | 76 (47 %) |
| Female | 87 (53 %) |
| **Primary Language** |  |
| English | 116 (71 %) |
| Spanish | 47 (29 %) |
| **Ethnicity** |  |
| Hispanic | 89 (55 %) |
| Black | 64 (39 %) |
| Caucasian | 7 (4 %) |
| East Indian | 1 (1 %) |
| Other | 2 (1 %) |

# of patients below 2 g dietary sodium per day 72 (44 %)
physicians. Recommendations for interventions such as implanted defibrillators or evaluation for cardiac transplantation result in referrals to the appropriate specialists.

In general, patients have been highly receptive to this type of intervention, in which the nurse serves as a navigator and advocate for their health care, and much of the program’s success can be attributed to the nurse’s skills as a listener. Psychosocial aspects of well-being are often revealed during personal visits and phone calls. Once trust is established, these disclosures often help enhance communication between the patient and the health care team.

Through programs like the Alliance for Health Improvement, Mount Sinai Heart is leading the way in managing chronic health problems among underserved populations. While physicians continue to play a major role in the longitudinal care of patients with cardiac disease, there is a clear need and expanding role for collaborative initiatives like this across a range of conditions.

The HEART program is located at the Diagnostic Treatment Center of Internal Medical Associates. The program is staffed by Ms. Elizabeth Vicente, RN, and cardiologist Mary Ann McLaughlin, MD, Associate Professor of Medicine (Cardiology) and Assistant Professor of Health Policy.

For further information about the referral criteria, contact Ms. Vicente at (212) 824-7509.

---

**ABOUT THE AUTHORS**

ELIZABETH SOCIAS VICENTE, RN, is Clinical Nurse, HEART Program, Heart Failure Education and Rehabilitation Training Internal Medicine Association, Center for Advanced Medicine.

MARY ANN McLAUGHLIN, MD, MPH, is Associate Professor of Medicine (Cardiology) and Health Policy.

EUNICE ALLEN, MPH, is Assistant Project Manager, Office for Excellence in Patient Care.

---

**REFERENCES**


Diagnosis and Management of Fetal Cardiac Arrhythmias

by BARRY A. LOVE, MD; SHUBHIKA SRIVASTAVA, MBBS; AVI FISCHER, MD; JOANNE STONE, MD; AND IAN H. HOLZMAN, MD

One in every 1,000 pregnancies is complicated by a serious fetal cardiac arrhythmia. To ensure optimal outcomes requires an integrated, multidisciplinary approach.

The obstetrician usually recognizes a fetal arrhythmia because of a persistent, abnormally high (>200 bpm) or low (<80 bpm) fetal heart rate or an irregular heartbeat beyond 16 weeks’ gestation. The electrocardiogram (ECG), the fundamental tool of rhythm diagnosis, cannot be used to assess the fetal rhythm, so the cardiologist must rely upon detailed echocardiography to assess the timing of mechanical contractions of the atria and ventricles of the fetal heart to establish the diagnosis. In addition to rhythm, fetal echocardiography assesses cardiac structure and function and helps to evaluate fetal well-being. Fetal magnetocardiography, a research technique that generates an ECG-like tracing of the fetal heart rhythm, may become a practical clinical tool in the future.

The most common fetal arrhythmias are premature atrial contractions (PACs), blocked PACs, and premature ventricular contractions (PVCs). These conditions, though benign, must be differentiated from more serious rhythm problems to avoid unnecessary concern and intervention.

**FETAL TACHYARRHYTHMIAS**

Fetal tachyarrhythmias may be incessant or episodic. When incessant, they ultimately lead to fetal hydrops, which is generalized fetal edema signifying serious impairment of fetal well-being, or fetal demise. The most common fetal tachyarrhythmia is AV-reciprocating tachycardia due to a bypass tract, characterized by a 1:1 AV ratio and a rate between 220–300 bpm. The second most common fetal tachyarrhythmia is atrial flutter (Figure 1), which accounts for about one-quarter of all fetal supraventricular tachycardia (SVT). In fetal life, this arrhythmia typically has a 2:1 AV ratio with an atrial rate just over 400 bpm and a ventricular rate of 220–240 bpm. Ventricular tachycardias are only rarely recognized in the fetus.

The treatment of fetal tachyarrhythmias depends on fetal maturity. Even in the absence of arrhythmia, survival of extremely premature infants without major morbidity is low, while outcomes beyond 33 weeks’ gestation are excellent (Table 1). The goal of therapy is to control the arrhythmia sufficiently to improve fetal well-being, allowing delivery and treatment of a term or near-term newborn. If the arrhythmia diagnosis is made beyond 36 weeks’ gestation, and the fetus faces compromise as a result of the arrhythmia, delivery and treatment of the newborn are indicated. When the fetus is less mature treatment is required—especially when there are signs of impending compromise.

The most common treatment of fetal tachyarrhythmias in utero is transplacental therapy, in which an antiarrhythmic drug is administered to the mother, relying on the placenta to transfer the drug to the fetus for the desired antiarrhythmic effect. Commonly used antiarrhythmic drugs for transplacental therapy include digoxin, flecainide, amiodarone, and sotalol. The pharmacokinetics of transplacental therapy are complex because the increased maternal volume of distribution, ratio of drug transported across the placenta, and impact of hydrops on placental drug transfer all affect dose requirements (Table 2). Avoiding maternal drug toxicity
requires frequent monitoring of the maternal ECG and serum levels of the drug and its principal metabolites. Digoxin is usually effective as monotherapy in the non-hydropic fetus, with rates of rhythm control approaching 80 percent, but this form of treatment is considerably less effective in the hydropic fetus when other drugs should be considered as first-line therapy.

DIRECT FETAL ADMINISTRATION OF ANTIARRHYTHMIC DRUGS

In the rare case of an immature fetus whose condition is deteriorating despite transplacental therapy, direct administration of antiarrhythmic medication to the fetus can be performed by injecting the drug into the umbilical cord, the fetal peritoneal cavity, or fetal thigh musculature. Adenosine has been administered directly into the umbilical cord; because of its very brief duration of action, tachycardia usually resumes shortly after termination. Direct intervention on the fetus risks induction of preterm labor, fetal injury, and infection.

BRADYARRHYTHMIAS

Congenital heart block is the most common cause of pathological fetal bradycardia, occurring in about 1 in 20,000 pregnancies. Typical heart rates in fetal complete heart block are below 80 bpm. With rates below 55 bpm, hydrops and fetal demise become considerably more likely. Maternal anti-Ro/anti-La antibodies, as occur in maternal systemic lupus erythematosus and other connective tissue diseases, are responsible for over 90 percent of cases of fetal heart block. These antibodies are transferred to the fetus after about 20 weeks’ gestation and have an affinity for the developing conduction system, leading to inflammation and cellular damage. It is important to note, however, that a mother with anti-Ro/anti-La antibodies faces only a 1-2 percent chance that her fetus will develop complete heart block; a mother who has had a previous infant with complete heart block has a 20-40 percent chance that a subsequent fetus will be similarly affected. In severely affected fetuses, cardiomyopathy may result from generalized inflammation of the myocardium.
A diagnosis of complete heart block can be made by fetal echocardiography, based on AV dissociation with a normal atrial rate and slow ventricular rate (Figure 2).

Transplacental administration of β-agonists improves outcome in fetuses with bradycardia resulting from complete heart block. Transplacental corticosteroid administration in cases of antibody-mediated fetal heart block. By employing echocardiographic techniques to detect first- and second-degree AV block, complete heart block has been avoided in some cases, with normalization of the AV interval after transplacental corticosteroid administration. Antenatal steroid therapy has been implicated, however, in the development of chorioamnionitis, fetal adrenal insufficiency, and impaired fetal somatic and brain development, preventing the widespread use of this approach.

### CASE EXAMPLE

The obstetrician of a 27-year-old primigravid mother noted a fetal heart rate of 240 bpm at 28 weeks’ gestation and referred the patient to the Mount Sinai Fetal Heart Program.

Echocardiography confirmed a persistent fetal tachyarrhythmia with a 1:1 AV relationship (Figure 3). Fetal sonography disclosed

---

**TABLE 2.** Drugs commonly administered to the mother to treat fetal arrhythmias

<table>
<thead>
<tr>
<th>Drug (oral administration)</th>
<th>Fetal:Maternal drug level</th>
<th>Fetal:Maternal drug level when hydrops present</th>
<th>Major risks (fetal and maternal)</th>
<th>Maternal monitoring</th>
</tr>
</thead>
<tbody>
<tr>
<td>Digoxin</td>
<td>0.6:1</td>
<td>0.2:1</td>
<td>Early maternal digoxin toxicity (nausea/vomiting)</td>
<td>ECG serum digoxin level</td>
</tr>
<tr>
<td>Sotalol</td>
<td>3:1</td>
<td>3:1</td>
<td>Increased risk of fetal demise (up to 25% in one series)</td>
<td>ECG (↑ QTc)</td>
</tr>
<tr>
<td>Flecainide</td>
<td>1:1</td>
<td>1:1</td>
<td>Risk of fetal demise (16% in one series)</td>
<td>ECG</td>
</tr>
<tr>
<td>Amiodarone</td>
<td>0.15:1</td>
<td>0.03:1</td>
<td>Transient neonatal hypothyroidism</td>
<td>ECG Thoracic function Transaminases</td>
</tr>
</tbody>
</table>

---

*despite lower ratio, clinically effective even in hydrops*
no evidence of fetal compromise or hydrops. The mother was hospitalized on the obstetrical service, where a normal baseline maternal ECG and electrolytes were verified and oral digoxin was administered at a dose of 0.5 mg every eight hours. After 48 hours, the dose was reduced to 0.5 mg twice daily, adjusted based on daily maternal serum digoxin measurements to achieve trough levels between 1.5 and 2 ng/ml. Daily obstetrical scans and fetal echocardiograms were performed to assess the arrhythmia burden and fetal well-being. By the third day, there were brief interruptions of the arrhythmia, and by the fifth day the arrhythmia was present 20-30 percent of the day. The mother was discharged and followed twice weekly. The fetal tachycardia density remained relatively low for the remainder of pregnancy with good fetal development, and spontaneous vaginal delivery was successful at term.

After delivery, the infant was admitted to the neonatal intensive care unit for monitoring. The initial ECG was normal in sinus rhythm. At two hours of life, persistent supraventricular tachycardia developed at a rate of 214 bpm (Figure 4).

The PR interval exceeded the RP interval with inverted P waves in the inferior leads, compatible with junctional re-entrant tachycardia. The rhythm was controlled with sotalol, and the infant was discharged on the tenth day. One year later, the child is developing normally, maintained on sotalol. It remains undetermined whether she will outgrow the arrhythmia or require ablation therapy in the future.

CONCLUSIONS

Recognition and treatment of cardiac arrhythmias in the fetus may avert fetal morbidity and mortality. A multidisciplinary approach that brings together the expertise of high-risk obstetricians, fetal echocardiographers, pediatric and adult cardiac electrophysiologists, and neonatologists provides the best opportunity to ensure optimum outcomes for both the mother and the fetus.

To learn more, visit www.mountsinai.org/pulse/FetalCardiacArrhythmias.
Barry A. Love, MD, is Assistant Professor of Pediatrics and Director of the Pediatric Arrhythmia Service.

Shubhika Srivastava, MBBS, is Associate Professor of Pediatrics and Director of the Pediatric and Fetal Echocardiography Laboratory, Division of Pediatric Cardiology.

Joanne Stone, MD, is Associate Professor of Obstetrics and Gynecology and Director of the Maternal & Fetal Medicine Program.

Avi Fischer, MD, is Assistant Professor of Medicine and Director of the Pacemaker and Defibrillator Center, Cardiac Electrophysiology Section, Cardiovascular Institute.

Ian R. Holzman, MD, is Chief, Division of Newborn Medicine; Vice-Chair for Clinical Affairs and Professor of Pediatrics.

To discuss a case or refer a patient for fetal heart evaluation, please contact Dr. Srivastava at (212) 241-8663.
Real-Time 3-Dimensional Intraoperative Transesophageal Echocardiography

by GREGORY W. FISCHER, MD

Echocardiography, a vital tool in contemporary cardiac anesthesiology, has evolved considerably since it was introduced over two decades ago. Among the most important advances has been progression from one-dimensional (A- and M-mode) imaging to two-dimensional (2-D) imaging, but three-dimensional (3-D) imaging of the heart could facilitate communication between the anesthesiologist (imager) and the cardiac surgeon about the structure and function of the heart before, during, and immediately after surgery.

A newly developed technology, based on a matrix array of piezoelectric crystals within the transducer, allows for real-time volumetric scanning, which enables acquisition of real-time 3-D ultrasound images.

Until recently, 3-D transesophageal echocardiography (TEE) in the operating room required acquisition of multiple, gated image planes under electrocardiographic and respiratory gating to overcome motion artifact. Views in the various imaging planes are acquired as the probe rotates 180° around the region of interest. The collected 2-D images are then post-processed and assembled to generate a 3-D image. The limitation of this technology is that it does not permit instantaneous, real-time imaging of the heart.

In the "live" mode, scanning takes place in real time, while an alternative "full volume" mode integrates 4–8 gated beats (as opposed to 90 beats), enabling generation of wider scan volumes while frame rate and resolution are maintained. In the live, real-time 3-D TEE mode, a volume pyramid is obtained, and the image changes as the transducer is moved, just as with 2-D imaging. Manipulation of the probe leads instantaneously to changes in the image visible on the monitor. In the "zoom" mode, also a "live-scanning" mode, a small magnified pyramidal volume can be displayed that varies in size from 20° × 20° to 90° × 90°, depending on the density setting. The resulting images are devoid of the rotational artifacts that are commonly encountered with other types of ECG-gated 3-D acquisition (Figure 1).

The main advantage of 3-D zoom mode is its ability to obtain detailed real-time assessment of the mitral valve apparatus. The relatively small data set can be spatially oriented to provide views of the valve from both the left atrial and left ventricular sides. The acquired real-time 3-D TEE data can subsequently be cropped, analyzed, and quantified using integrated software (Figure 2).

FACTORS AFFECTING IMAGE RESOLUTION

Echocardiographic image resolution is limited by the speed of sound rather than by computer processing power. A frame rate over 20 Hz allows insufficient time for sound to travel back and forth in large quanta while maintaining resolution in live scanning modes. One way to overcome this limitation involves combining blocks of 4–8 gated images to create "subvolumes" or "slabs" of data to reconstruct the pyramidal data set that is generated directly in the live 3-D mode. By this technique, scanning volumes > 90° can be generated at frame rates over 30 Hz. Increasing the number of gated segments from four to eight creates smaller 3-D slabs, which can then be used to maintain frame rates and/or resolution as the volume pyramids become larger.

GATED 3-D COLOR DOPPLER IMAGING

Color-flow Doppler echocardiography requires multiple samples obtained along a common scan line, and the velocity of moving tissue or blood is derived from frequency shifts of reflected...
sound waves. The short wavelengths required to detect shifts at high frequencies along a stationary scan line deteriorates frame rate, and to compensate for this a gating method similar to the full-volume mode is required. Because of the large amount of data required, 8–11 beats must be combined to create an image sufficient to determine jet direction, magnitude, and geometry. A special strength of 3-D acquisition is its ability to quantify mitral regurgitation, which correlates better with angiographic measurements than does 2-D imaging, which tends to underestimate regurgitant volume.

Cardiac anesthesiologists at Mount Sinai Heart were among the first to test this new technology, which is employed routinely to obtain better understanding of complex mitral and congenital lesions and to improve the assessment of ventricular function.

> FIGURE 1. REAL-TIME 3-D INTRAOPERATIVE ECHOCARDIOGRAPHIC IMAGE ACQUIRED IN THE “LIVE” MODE SHOWING A VOLUMETRIC PYRAMID. LV DENOTES LEFT VENTRICLE; RV, RIGHT VENTRICLE AND LVOT, LEFT VENTRICULAR OUTFLOW TRACT.

> FIGURE 2. INTRAOPERATIVE ECHOCARDIOGRAPHIC IMAGE OF THE MITRAL VALVE CORRESPONDING TO THE SURGEON’S VIEW, ACQUIRED IN THE “ZOOM” MODE. THE DATA ARE SPATIALLY ORIENTED WITH THE AORTIC VALVE POSITIONED AT THE TOP. MEDIAL PROLAPSE OF THE P2 SCALLOP OF THE POSTERIOR LEAFLET OF THE MITRAL VALVE IS EVIDENT WITH RUPTURED CHORDAE TENDINEAE.

> ABOUT THE AUTHOR

GREGORY W. FISCHER, MD,

is Associate Professor of Anesthesiology and Cardiothoracic Surgery.

> REFERENCES

Clinical Trials Update

There are over 45 active studies at Mount Sinai Heart, ranging from the evaluation of new diagnostic techniques to novel therapies for the treatment and prevention of cardiovascular disease. With 75 full-time employees, the Clinical Trials Unit provides clinical and academic expertise to support the development, implementation, and successful conclusion of cardiovascular clinical trials sponsored by the National Institutes of Health, Mount Sinai School of Medicine, the pharmaceutical industry, and national organizations and foundations. Two trials are summarized here.

VIA FDG-PET

A randomized, double-blind, placebo-controlled trial to study reduction in plaque inflammation and biomarker measurements of inflammation.

Embodying the interdepartmental collaboration that is central to Mount Sinai Heart, the VIA FDG-PET study brings together our trials and cardiovascular imaging infrastructure to evaluate a potent small-molecule drug that targets inflammation in the blood vessel wall. The use of state-of-the-art FDG-PET imaging technology provides a new and important methodology for measuring the effect of VIA-2291 in reducing vascular inflammation.

VIA-2291 is under development as a once-daily, oral agent to decrease the risk of major adverse cardiovascular events associated with inflammation, including heart attack and stroke. The VIA FDG-PET study is a 24-week, randomized, double-blind, placebo-controlled phase 2 trial enrolling approximately 50 patients following myocardial infarction. Endpoints include reduction in plaque inflammation following dosing with VIA-2291 as measured by FDG-PET, as well as standard biomarker measurements of inflammation. The trial will complete recruitment in the spring of 2009, and results are expected in late 2009.

**Main Inclusion Criteria:** Recent acute coronary syndrome (ST elevation myocardial infarction [STEMI], non-STEMI or unstable angina) documented by ECG, cardiac enzymes, or angiogram 1–3 months prior to randomization.

**Main Exclusion Criteria:** Uncontrolled Type 2 diabetes defined as hemoglobin A1c level >9 percent, New York Heart Association Class III or IV heart failure, or renal insufficiency (serum creatinine >1.5 x the upper limit of normal).

A second trial, sponsored by Merck, will evaluate the differences in plaque inflammation between treatment with high- versus low-dose statins in patients with documented atherosclerotic disease. This trial will attempt to validate the FDG-PET as an imaging biomarker and provide important insights into early effects of high-dose statins in a stable cardiovascular population.

COAG

A randomized controlled trial to clarify optimal anticoagulation through genetics.

Sponsored by the National Institutes of Health, National Heart, Lung & Blood Institute, this multicenter trial of approximately 1,250 patients will be conducted over about two years beginning in April 2009. The study brings together the expertise of the Department of Genetics & Genomic Sciences and the Cardiovascular Institute.

The objective is to determine whether using a genetics-guided algorithm to determine initial warfarin dose improves the amount of time that anticoagulation intensity is maintained in the therapeutic range during the first month of therapy. Patients who are beginning therapy with warfarin will be randomized to an initial dose for the first five days that is based on clinical data alone or clinical data plus genetic information (polymorphisms in genes that affect warfarin sensitivity).

**Main Inclusion Criteria:** Initiating warfarin therapy with an intended duration of at least three months; target INR of 2-3; to be followed in a Mount Sinai Anticoagulation Clinic.

**Main Exclusion Criteria:** Currently taking warfarin therapy or prior known stable warfarin dose; abnormal baseline INR; need for warfarin to be adjusted for reasons not accounted for by dosing algorithm.

For more information about these or other trials, contact Dr. Michael E. Farkouh at (212) 659-9181 or e-mail michael.farkouh@mssm.edu.
New Faces

Adult Cardiology

KEVIN G. DUNSKY, MD, FACC,
Associate Professor of Medicine, Director, Cardiovascular Practice Development

UMESH GIDWANI, MD, FCCP,
Assistant Professor of Medicine, Director, Cardiac Critical Care

LYNNE A. GLASSER, MD,
Assistant Professor of Medicine, Director, Interventional Cardiology Inpatient Service

AJITH NAIR, MD,
Clinical Instructor in Medicine, Director, Pulmonary Hypertension Program

TIMOTHY VITTORIO, MS, MD,
Assistant Professor of Medicine, Associate Director, Heart Failure Program

JOSE M. WILEY, MD, FACC, FSCAI,
Assistant Professor of Medicine & Radiology, Associate Director of Endovascular Intervention, Director, Cardiac Catheterization Laboratory, North General Hospital

Pediatric Cardiology

SUJATA CHAKRAVARTI, MD,
Assistant Professor of Pediatrics

MIWA GEIGER, MD,
Assistant Professor of Pediatrics

JAMES NIELSON, MD,
Associate Professor of Pediatrics, Director, Pediatric Non-Invasive Cardiac Imaging Laboratory

Vascular Surgery

ROWAN WALSH, MB, BAO, BCH,
Assistant Professor of Pediatrics

AGELIKI G. VOYOUKA, MD, FACS,
Assistant Professor of Surgery and Radiology
# CME Calendar of Events

Continuing medical education is a priority at Mount Sinai Heart, and these sessions provide an opportunity for faculty and fellows to interact with visiting physicians and other health care professionals. The institute sponsors nearly 50 lectures, conferences, and academic rounds every month, and we invite you to share in these special educational events as often as you can. For information about conference locations or an updated schedule, please contact Ms. Imelda Samson at (212) 241-7784 (imelda.samson@mountsinai.org).

## PROGRAM HIGHLIGHTS: CARDIOLOGY CONFERENCES

### Visiting Professors

<table>
<thead>
<tr>
<th>Date</th>
<th>Professor</th>
<th>Institution</th>
</tr>
</thead>
<tbody>
<tr>
<td>September 21, 2009</td>
<td>Joseph Loscalzo, MD</td>
<td>Brigham and Women’s Hospital, Harvard Medical School</td>
</tr>
<tr>
<td>October 26, 2009</td>
<td>Robyn J. Barst, MD</td>
<td>Columbia University and Cornell Medical Center</td>
</tr>
<tr>
<td>November 30, 2009</td>
<td>Peter Libby, MD</td>
<td>Brigham and Women’s Hospital, Harvard Medical School</td>
</tr>
<tr>
<td>December 28, 2009</td>
<td>Jagat Narula, MD</td>
<td>University of California, Irvine</td>
</tr>
<tr>
<td>January 25, 2010</td>
<td>Christopher O’Connor, MD</td>
<td>Duke University</td>
</tr>
</tbody>
</table>

## DAILY/WEEKLY CONFERENCES

### Mondays

- **@7:45 am** Coronary Care Unit
- **@5:00 pm** Cardiology Grand Rounds

### Tuesdays

- **@7:15 am** Catheterization Laboratory
- **@12:00 pm** Electrocardiography
- **2nd, 4th, & 5th weeks @7:15 am** Interventional Cardiology Journal Club
- **1st, 2nd, & 5th weeks @7:45 am** Catheterization Laboratory

### Wednesdays

- **1st week @6:30 am** Interventional Research
- **2nd week @12:00 pm** Cardiovascular Pathology
- **4th week @12:00 pm** Hemodynamics Rounds

### Thursdays

- **@7:15 am** Coronary Anatomy lecture
- **@7:45 am** Fellows Rounds with Valentin Fuster, MD, PhD
- **@12:00 pm** Clinical Cardiology with José Meller, MD

### Fridays

- **2nd week @7:15 am** High-Risk CT & PCI
- **@7:45 am** Journal Club

## OTHER DAILY/WEEKLY CONFERENCES

### Anesthesiology Grand Rounds

- **Wednesday @6:45 am** Clinical Case Conference

### Cardiothoracic Surgery

- **2nd Wednesday @8:00 am** Quality Assurance Conference
- **1st, 4th, & 5th Wednesdays @8:00 am** Clinical Conference

### Nursing

- **October 2009** Nurse Practitioner Cardiovascular Symposium

### Vascular Surgery

- **Mondays @7:00 am** Clinical Case Presentations
- **3rd Fridays @7:00 am** Journal Club
- **Fridays except 3rd @7:00 am** Conjoint Vascular Medicine, Interventional, and Radiology Conference

### Pediatric Cardiology

- **Mondays and Fridays @9:00 am** Multidisciplinary rounds
- **Tuesdays @8:00 am** Didactics
- **3rd Tuesday @8:00 am** Echocardiogram Lab Q & A
- **Last Tuesday @8:00 am** Pediatric Echocardiography Conference
- **Wednesdays @3:00 pm** Pediatric Echocardiography Conference
- **Conjoint Pediatric and Adult Cardiology and Cardiothoracic Surgery Conference on Congenital Heart Disease**
- **Wednesdays @5:00 pm (except 2nd Wednesday)** Echocardiography and congenital heart disease conference

### Pediatric Cardiology Journal Club

- **2nd Thursday @4:00 pm** Pediatric Cardiology Journal Club
- **3rd & 4th Thursdays @4:00 pm** Pediatric Cardiology Core Curriculum
2009 Live Symposium of Complex Coronary and Cardiovascular Cases

Emphasizing the intricate details of the procedural techniques, Mount Sinai Heart’s 12th Annual Live Symposium of Complex Coronary and Cardiovascular Cases focused on a multimodality approach to revascularization of patients with complex arterial disease.

The symposium, held June 17–20, included 23 live cases with panel discussions highlighting treatment of chronic total arterial occlusion, unprotected left main and bifurcation coronary lesions, left ventricular assist device support, and treatments for renal, femoral, and infra-popliteal arterial disease.

Directed by Samin K. Sharma, MD, and Annapoorna S. Kini, MD, this continuing medical education program brought over 525 physicians, nurses, and technicians to New York City to learn the latest techniques in interventional cardiology. In addition to Mount Sinai faculty, guest faculty included 23 renowned interventional cardiologists from across the United States, as well as India, England, and Japan, bringing a global perspective.

For more information about this symposium, please visit www.mountsinai.org/pulse/cccsymposium.

In the next PULSE
A focus on electrophysiology

With the arrival of Vivek Y. Reddy, MD, as Director of the Electrophysiology Laboratories at Mount Sinai Heart, this institution will expand its services for heart-rhythm disorders. The next Pulse will describe some of the new programs Mount Sinai Heart will introduce to the field of cardiac rhythm disorders.
<table>
<thead>
<tr>
<th>Mount Sinai Heart Telephone Numbers (Area Code 212)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MS Heart Director</strong></td>
</tr>
<tr>
<td><strong>Cardiac Anesthesiology</strong></td>
</tr>
<tr>
<td><strong>Cardiac Health Program</strong></td>
</tr>
<tr>
<td><strong>Cardiothoracic Surgery</strong></td>
</tr>
<tr>
<td><strong>Cardiac Nursing</strong></td>
</tr>
<tr>
<td><strong>Cardiovascular MRI &amp; CT Imaging</strong></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td><strong>Catheterization Laboratories</strong></td>
</tr>
<tr>
<td><strong>Clinical Trial Unit</strong></td>
</tr>
<tr>
<td><strong>Consultation Service</strong></td>
</tr>
<tr>
<td><strong>Coronary Care Unit</strong></td>
</tr>
<tr>
<td><strong>Development</strong></td>
</tr>
<tr>
<td><strong>Echocardiography</strong></td>
</tr>
<tr>
<td><strong>Electrophysiology</strong></td>
</tr>
<tr>
<td><strong>Genetic Disorders</strong></td>
</tr>
<tr>
<td><strong>Heart Failure &amp; Transplantation</strong></td>
</tr>
<tr>
<td><strong>Lipid Management</strong></td>
</tr>
<tr>
<td><strong>Nuclear Cardiology &amp; Stress Testing</strong></td>
</tr>
<tr>
<td><strong>Pediatric Cardiology</strong></td>
</tr>
<tr>
<td><strong>Pulmonary Hypertension</strong></td>
</tr>
<tr>
<td><strong>Telemetry Unit</strong></td>
</tr>
<tr>
<td><strong>Vascular Laboratory</strong></td>
</tr>
<tr>
<td><strong>Vascular Medicine</strong></td>
</tr>
<tr>
<td><strong>Vascular Surgery</strong></td>
</tr>
<tr>
<td><strong>Vein Program</strong></td>
</tr>
<tr>
<td><strong>Women’s CARE</strong></td>
</tr>
</tbody>
</table>