Severe, untreated mitral regurgitation (MR) leads to progressive left ventricular (LV) dysfunction and heart failure, with mortality for symptomatic patients of at least 5% annually. "Aggressive medical management may attenuate symptoms but does not change mortality figures" says Vuyisile T. Nkomo MD, codirector of the Valvular Heart Disease Clinic at Mayo Clinic in Rochester. The only definitive treatment is operative, with mitral valve repair or replacement. American College of Cardiology/American Heart Association (ACC/AHA) guidelines recommend surgery for moderate-to-severe or severe MR in symptomatic patients and those with evidence of LV dysfunction. Unfortunately, many of the most symptomatic patients are elderly and medically fragile and not candidates for surgical repair. The recent ACC/AHA 2014 guidelines now recommend transcatheter mitral valve repair for individuals with primary or degenerative MR and prohibitive surgical risk (IIb).

The early percutaneous approach to mitral valve disease focused on the treatment of mitral stenosis with balloon valvuloplasty; more recently, paravalvular leaks have been closed with percutaneous occlusive devices. Percutaneous correction of MR has been more challenging. "Current procedures target leaflet modification; various percutaneous annuloplasty approaches are under investigation, but most are in early stages of development," according to Guy S. Reeder, MD, interventional cardiologist at Mayo Clinic in Rochester. "Treatment of MR with percutaneous coronary sinus annuloplasty is intuitively attractive, but there are technical limitations."

The anatomic relationship of the coronary sinus to the valve annulus is highly variable, and the coronary sinus frequently runs along the atrial side rather than in the true plane of the annulus. "In more than half of patients, branches of the circumflex artery run beneath the coronary sinus; tightening a percutaneous annuloplasty ring in the coronary sinus may compress the circumflex artery, inducing myocardial ischemia or infarction," says Mackram F. Eleid, MD, interventional cardiology fellow at Mayo Clinic in Rochester. "Preprocedural imaging studies have not reliably defined the relationship between the mitral valve annulus, the circumflex artery, and the coronary sinus, nor have..."
Percutaneous leaflet modification has been more promising. Two percutaneous devices have been developed; conceptually, both techniques were derived from the Alfieri surgical repair, in which a mid-leaflet suture creates a double orifice valve. One device used a transseptal suction catheter to approximate the mitral leaflets and deploy cutaneous sutures. Trials demonstrated feasibility, but this approach was abandoned as the procedure was technically difficult. The current approach to percutaneous leaflet modification uses the MitraClip device (Abbott Vascular, Santa Clara, California), which fixes or “clips” the anterior and posterior mitral leaflets together under transesophageal echocardiographic (TEE) guidance. The MitraClip device is 4 mm wide and made of cobalt-chromium; its 2 arms or clips are opened and closed by a handle on the delivery catheter. Like the Alfieri procedures, a double-orifice valve is created (Figure 1). Importantly, the clip can be surgically removed and does not preclude later surgical treatment if warranted. Animal studies suggest that the clip becomes encapsulated within 3 months after implantation. MitraClip has been CE mark–approved for clinical use in Europe since 2005, where more than 8,000 patients have been treated in the past decade.

The Endovascular Valve Edge-to-Edge Repair Trials (EVEREST I and EVEREST II) evaluated the safety and efficacy of the MitraClip in high-risk patients with severe MR. EVEREST I was a feasibility trial; 55 patients were enrolled and 49 received the device. EVEREST II evaluated patients from 37 centers in Canada and the United States. Patients with MR were symptomatic and had LV ejection fraction greater than 25% and LV end-systolic diameter of 55 mm or less. Asymptomatic patients had to have LV ejection fraction of 25% to 60%, LV end-systolic diameter of 40 to 55 mm, new atrial fibrillation, or pulmonary hypertension to enroll. A total of 279 patients were randomly assigned in a 2:1 ratio to receive the MitraClip vs standard surgery. The primary composite end point was freedom from death, subsequent surgery for MR, and grade 3+ or 4+ MR at 1 year.

Researchers found that the 30-day mortality rate for MitraClip was much lower than that for surgery (4.8% vs 18.2%), with a 96% implant success rate and a low rate of adverse events. Importantly, patients identified major improvements in quality of life; also noted was a significant reduction in LV size and hospitalization rates during the first year after MitraClip placement compared with the prior year. However, 20% of individuals who received the MitraClip required operative repair of the valve within the first year because of persistent or recurrent MR, compared with 2.2% in the surgery group. The ongoing EVEREST registry and the European experience may provide data on the long-term durability of MitraClip repair.

The MitraClip is approved by the US Food and Drug Administration to treat patients with severe symptomatic primary/degenerative MR who would be too high risk for surgery. For patients with severe secondary/functional MR, the MitraClip is available through participation in the Clinical Outcomes Assessment of the MitraClip Percutaneous Therapy for Extremely High-Surgical-Risk Patients (COAPT) trial, in which patients are randomly assigned to receive the device or medical therapy.

At Mayo Clinic, candidates for MitraClip are evaluated by a multidisciplinary team of imaging specialists, interventionalists, and cardiac surgeons; there is no prespecified STS threshold for risk. Standard evaluation of valve suitability involves TEE assessment of the regurgitant mechanism and location and the technical suitability of valve morphology, including leaflet coaptation length. The procedure is performed in the cardiac catheterization laboratory under general anesthesia using TEE guidance. Access is percutaneous via the right femoral vein, with most patients discharged on postprocedure day 1 or 2. Patient experience with the procedure has been favorable, with minimal access site discomfort and rapid recovery (Figure 2).

For more information about MitraClip protocols at Mayo Clinic, please contact the Valvular Heart Disease Clinic at Mayo Clinic in Rochester at 507-266-4044.
Leadless Pacing Available for Selected Patients

Early pacing devices offered single-chamber, fixed-rate ventricular pacing for life-threatening conduction system disease. Advances in generator and lead technology and the results of clinical trials over the past 60 years have expanded the indications for device therapy. As a result, more individuals are receiving device therapy; approximately 190,000 pacemakers are implanted every year in the United States. Over time, the patient population receiving pacing therapy has become older and more complex.

The “weak link” in device therapy has been the leads. While transvenous leads typically have lower thresholds and better longevity than epicardial leads, they are associated with increased morbidity and mortality. Complications at implant include bleeding, vascular damage, cardiac perforation, pneumothorax, and dislodgment. Potential long-term concerns include lead fracture, malfunction, venous obstruction, tricuspid valve regurgitation, and the risks associated with lead extraction. Transvenous leads are contraindicated in the presence of right-to-left shunt and in some patients with congenital heart disease.

The concept of leadless pacing was first proposed in 1970 by Spickler and colleagues, but it is only recently that leadless devices have become available. Currently available are the Nanostim leadless pacemaker (St. Jude Medical, St. Paul, Minnesota) and the Micra transcatheter pacing system (Medtronic, Minneapolis, Minnesota); both are dime-sized capsules that are implanted directly into the right ventricular apex (Figures 1 and 2). The Nanostim uses active fixation, while the Micra has a tined fixation mechanism to secure the device to the right ventricular endocardial surface. Both devices are capable of VVIR pacing and have estimated battery longevity between 7 and 10 years. When the battery is depleted, a new device can be implanted and the existing device left in place.

These devices are contraindicated in individuals who require dual-chamber pacing or who have demonstrable pacemaker syndrome. Anticoagulation is not required after implant placement. Current devices are not MRI compatible. Leadless pacemakers are contraindicated in patients with implantable cardioverter-defibrillators, as high-voltage shocks could damage the pacemaker, and the effect of the pacemaker on shock effectiveness is unknown. Leadless devices should be avoided in individuals with elevated right ventricular pressures because of higher theoretical risk of embolization. The presence of mechanical tricuspid valves or inferior vena cava filters also precludes the use of leadless pacemakers. Successful device retrieval has been accomplished in animal studies.

For more information or to refer a potential candidate for leadless pacing, please contact Paul A. Friedman, MD, director, or Yong-Mei Cha, MD, codirector of the Heart Rhythm Device Clinic, at 507-255-4244.

Figure 1. Two currently available leadless pacing devices.

Nanostim (St. Jude Medical)  Micra (Medronic)

Figure 2. PA chest x-ray showing leadless pacemaker in right ventricle (arrow).
Implantable Loop Recorders in Patients With Cryptogenic Stroke

Stroke is a major cause of disability and death. Many strokes have a likely explanation, such as carotid disease, poorly controlled hypertension, diabetes, hyperlipidemia, smoking, inherited blood clotting conditions, and atrial fibrillation (AF). However, a quarter of patients have none of the defined risk factors and yet face the consequences of stroke or transient ischemic attack (TIA; stroke with resolution of symptoms within 24 hours). These cryptogenic strokes (no specific risk factor or cause found) create anxiety as it is unclear what can be done to prevent additional strokes. Cryptogenic strokes have been shown to have a higher rate of recurrence than other strokes.

AF causes approximately one-sixth of all strokes, and anticoagulation substantially lowers the risk of stroke in patients with AF. AF can be intermittent, short lived, and asymptomatic, making it challenging to identify the arrhythmia with conventional electrocardiography, ambulatory monitoring, and a 30-day event recorder. However, if a patient is detected to have AF and has a CHA2DS2-VASc score higher than 2, then there is compelling evidence that anticoagulation, with either warfarin or novel anticoagulants, reduces the stroke risk by approximately 65% (Table). One study conducted in patients with implanted pacemakers documented that stroke risk was significantly increased in those individuals with AF lasting more than 6 minutes (N Engl J Med 2012;366:120-129).

Asymptomatic AF as a risk factor for stroke is frequently considered but difficult to prove. “An implanted device is vastly superior to surface monitoring in detecting AF owing to continuous analysis over years, generally better signal-to-noise ratio, and lack of compliance issues frequently encountered with the use of external recorders,” says Komandoor Srivathsan, MD, director of Heart Rhythm Services at Mayo Clinic in Arizona. “Even among implantable devices, intracardiac electrogram acquisition through a pacemaker or an implantable cardiac defibrillator has more sophisticated rhythm recognition capabilities because of the spatial clarity of the obtained electrogram when compared with the subcutaneous recording of an implanted loop recorder.”

Many cryptogenic strokes are thought to be related to unrecognized AF. The use of implantable cardiac monitoring (ICM) to identify asymptomatic AF and associated stroke risk was explored in a recently published study (N Engl J Med 2014;370:2478-2486). This study indicated that an additional 10% of patients with AF can be detected at 12 months of ICM compared with other monitoring techniques, and more widespread use of ICM in individuals with cryptogenic stroke might allow for earlier identification of AF and anticoagulation treatment. This hypothesis is tempered by the following issues:

1. Ten patients have to have ICM to detect 1 additional patient with AF. Assuming therapeutic anticoagulation is of equal benefit to symptomatic AF patients at the time of stroke, approximately 100 patients will have to be implanted with a device to prevent 1 recurrent stroke (currently cost-prohibitive).
2. Infection, extraction, and reimplantation add to morbidity and cost.
3. Device detection issues and the occurrence of asymptomatic 30-second episodes of AF remain a concern.
4. The same issue of the journal reported that a 30-day event recorder was able to detect AF in a significant number of patients and minimized the need for ICM.
5. Competing risk factors are frequent in the age group of patients who experience stroke, and the etiology of a specific stroke ascribable to a cause is nebulous in many instances.

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<th>Table. CHA2DS2-VASc Scoring System</th>
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<td><strong>Congestive heart failure</strong></td>
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6. The majority of cryptogenic strokes remain cryptogenic even after these investigations. Nevertheless, this study adds important information that some cryptogenic stroke patients likely have AF, and AF should be high on the list of differential diagnoses in these individuals. The prevention of recurrent strokes in these patients is feasible through enhanced detection provided by ICM, but the subset of patients who would benefit from intensive monitoring needs to be better defined. Additional studies will need to confirm that anticoagulation is of equal benefit to those with cryptogenic stroke due to asymptomatic AF prior to its widespread adoption. The ICM size has recently been greatly reduced to the size of a large capsule, and implantation techniques have become simpler. Implantation of these smaller devices may eventually become an in-office, outpatient procedure, which would change the cost-benefit equation.

Summary Points

- Implantable cardiac monitoring with a subcutaneous loop recorder can detect asymptomatic, subclinical atrial fibrillation in 10% of patients with cryptogenic stroke at 1 year.
- The rate of detection of asymptomatic atrial fibrillation in cryptogenic stroke through implantable cardiac monitoring is low.
- The number of patients who need to receive implants to detect atrial fibrillation in cryptogenic stroke and prevent recurrence is currently too high to be cost-effective.

**RECOGNITION**

The Department of Medicine at Mayo Clinic in Rochester has announced 2014 award recipients. All are members of the Division of Cardiovascular Diseases.

George M. Gura, MD, received the Laureate Award, presented for professional excellence and personal integrity.

Samuel J. Asirvatham, MD, received the Outstanding Investigator Award; recipients have primary research appointments, and the award is based on scientific accomplishments, publications, and grant support.

Amir Lerman, MD, received the Teaching Excellence Award, given to young faculty whose work has led to important new insights in the field of biomedical science.

Joerg Herrmann, MD, received the New Investigator Award, presented for professional excellence and personal integrity.

Carole A. Warnes, MD, received the Lifetime Achievement Award for Outstanding Contributions to Medical Education. This honor is given for a career-long commitment to medical education that has resulted in substantial and enduring impact at national and international levels.

**NEW STAFF**

David L. Joyce, MD, has joined the Division of Cardiovascular Surgery at Mayo Clinic in Rochester. Dr. Joyce graduated from the US Air Force Academy and Harvard Medical School. He did his general surgery fellowship at Johns Hopkins University and his cardiovascular surgery fellowship at Stanford University. His areas of interest include heart and lung transplantation, mechanical circulatory support, and minimally invasive coronary surgery.
Arm Ergometer Provides Alternative to Conventional Stress Testing

The arm ergometer (also referred to as an “arm cycle” or “arm crank”) is a valuable alternative to the treadmill or leg cycle ergometer for exercise testing. In the arm ergometer stress test, the patient can sit or stand while cranking the arm ergometer (Figures 1 and 2). The test protocol is graded, just as a treadmill protocol, with increases in workload every 2 minutes until exhaustion. Either of 2 protocols may be used—one more vigorous and the other less so—depending on the age, sex, and activity level of the patient.

Peak oxygen consumption on the arm ergometer is approximately 65% of treadmill peak oxygen consumption and 70% of leg cycle peak oxygen consumption on account of the small exercising muscle mass. However, the peak heart rate reaches 90% to 95% of predicted with peak systolic blood pressure reaching 80% to 85% of what is typically achieved on the treadmill. Thus, the double product is generally high enough to bring out ischemic changes.

One obvious and well-studied application for arm ergometer stress testing is for patients with paraplegia or other severe lower extremity disability. The advantages of arm ergometry vs pharmacologic stress testing for these patients are that heart rate and blood pressure responses can be evaluated and that exercise capacity and symptoms can be quantified.

Another use of arm ergometry is for testing patients who complain of symptoms only or primarily during arm work, a not uncommon presentation in clinical practice. Arm working capacity, as measured during arm ergometry, has been shown to correlate more strongly than functional aerobic capacity or peak V̇O₂ from treadmill testing with performance on tasks such as shoveling, repetitive lifting, and carrying loads. Furthermore, arm exercise is characterized by reduced preload compared with leg exercise, as the lower limbs can act as a passive reservoir of blood, but afterload is elevated because of muscular contractions in the upper extremities.

These hemodynamic aspects of arm work explain the generation of angina despite lower overall workload compared with walking. Arm ergometry stress testing can be performed with or without simultaneous measurement of oxygen consumption.

For information about arm ergometry or any form of stress testing, please contact Thomas G. Allison, PhD, MPH, director of the Integrated Stress Center at 507-284-6320 or allison.thomas@mayo.edu.
Bernard J. Gersh, MB, ChB, DPhil, David R. Holmes Jr, MD, and Veronique L. Roger, MD, cardiologists at Mayo Clinic in Rochester, have been included on the list of “The World’s Most Influential Scientific Minds,” published by Thomson Reuters.

Mayo Clinic Program for Hypoplastic Left Heart Syndrome’s 2nd Annual

FEEL THE BEAT
Saturday, November 8, 2014
Mayo Clinic
Rochester, MN

Check out our blog @ http://nlhsblog.mayoclinic.org/

Bernard J. Gersh, MB, ChB, DPhil, a cardiologist at Mayo Clinic in Rochester, has received honorary membership in the British Cardiovascular Society. Honorary membership recognizes esteemed individuals who have made an outstanding contribution to the practice of cardiology worldwide and who are held in high regard by the British cardiology community.

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Mayo Clinic is honored to be ranked as U.S. News & World Report’s top hospital. Mayo Clinic in Minnesota is also recognized as one of the top Cardiology & Heart Surgery hospitals in the nation for 2014-2015 by U.S. News & World Report.

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Apr 25-28, 2015, Rochester, MN

Echocardiography in the Nation’s Capital:
Focus for the Physician and Sonographer
May 8-10, 2015, Washington, DC

Basic to Advanced Echocardiography:
From the Blue Ridge Mountains of Asheville
May 13-16, 2015, Asheville, NC

Cardiac Rhythm Device Summit
Implantation, Management, and Follow-up
Jun 26-28, 2015, Chicago, IL

29th Annual Echocardiographic Symposium at Vail:
New Technologies, Live Scanning, and Clinical Update
Jul 20-23, 2015, Vail, CO

Success With Failure: Strategies for the Evaluation
and Treatment of Heart Failure in Clinical Practice
Aug 10-12, 2015, Dana Point, CA

Cardiovascular Board Reviews
Aug 22-27, 2015, Rochester, MN

Challenges in Clinical Cardiology:
A Case-Based Update
Sep 18-20, 2015, Chicago, IL

Mayo Clinic Interventional Cardiology Board Review
Sep 25-27, 2015, Rochester, MN

Advanced Catheter Ablation: New Tips, Techniques,
and Technologies for Complex Arrhythmia
Oct 2-6, 2015, Washington, DC

31st Annual Echocardiography in
Pediatric and Adult Congenital Heart Disease
Oct 8-11, 2015, Phoenix, AZ

Electrophysiology Review for Boards
and Recertification
Oct 9-11, 2015, Rochester, MN

Cases in Echocardiography, Cardiac CT and MRI
Oct 21-24, 2015, Napa, CA

Coronary Artery Disease: Prevention,
Detection, and Treatment
Nov 20-22, 2015, Las Vegas, NV

5th Annual Echo on Marco Island:
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Dec 3-6, 2015, Marco Island, FL

8th Annual The Heart Beat of Cardiology:
Practical Application of Echocardiography
Dec 10-12, 2015, Chicago, IL

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Dec 4-7, 2014, Phoenix, AZ

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Application of Echocardiography
Dec 11-13, 2014, Chicago, IL

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Jan 7-10, 2015, Miami Beach, FL

Hawaii Heart 2015: Echocardiography
and Multimodality Imaging: Case-Based
Clinical Decision Making
Jan 26-30, 2015, Wailea, Maui, Hawaii

22nd Annual Arrhythmias and the
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Feb 2-6, 2015, Kauai, Hawaii

40th Annual Cardiovascular
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Feb 13-16, 2015, Snowbird, UT

Heart Failure Management for Nurse
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Mar 26-29, 2015, San Antonio, TX

4th Annual Innovations in Valve
and Structural Heart Disease
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Mayo Clinic Cardiovascular Reviews in Bahrain
Mar 25-28, 2015, Manama, Bahrain

5th Annual Echo on Marco Island:
Case-Based Approach
Dec 3-6, 2015, Marco Island, FL

8th Annual The Heart Beat of Cardiology:
Practical Application of Echocardiography
Dec 10-12, 2015, Chicago, IL

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