The year 2003 marked the 50th anniversary of the introduction of clinical cardiac echocardiography. Mayo Clinic in Rochester commemorated the event with a 2-day program and gala dinner on October 11 and 12, 2003, attended by more than 140 people from around the world, many of whom were instrumental in the development of this important technique. Pioneer Harvey Feigenbaum, MD, served as the keynote speaker.

The science and art of echocardiography were first developed by the Swedish cardiologist Inge Edler and physicist Carl Hellmuth Hertz on a borrowed industrial ultrasonography machine. Drs Edler and Hertz began their work at Lund University in Sweden in 1953 and published their initial observations the following year. Echocardiography was introduced in the United States in the early 1960s by cardiologists Claude Joyner from the University of Pennsylvania and Harvey Feigenbaum from Indiana University. In the late 1960s, echocardiography was introduced at Mayo Clinic by cardiologist Thomas T. Schattenberg, MD (Figure 1).

In the early years, echocardiographic data were presented on an oscilloscope as an amplitude signal (A mode), which had the appearance of dancing bright specks of light. By 1972 strip chart records displayed motion waves (M mode) on light-sensitive paper (Figure 2). “The A-mode and M-mode data were unfamiliar to most cardiologists and bore little resemblance to actual cardiac anatomy, and it was necessary to have an expert echo physician interpret the recording,” says A. Jamil Tajik, MD, former director of the echocardiography laboratory at Mayo Clinic in Rochester and former chair of the division of cardiology. “By the mid 1970s, 2-dimensional (2-D) echocardiography had revolutionized noninvasive imaging by displaying tomographic images of the heart.” These images more clearly portrayed actual cardiac anatomy and function and led to phenomenal growth in the use echocardiographic technology, including:

- Spectral Doppler echocardiography allows noninvasive measurement of blood flow, stroke volume, cardiac output, valvular pressure gradients, valve function, and cardiac pressures.
- Color flow Doppler imaging permits noninvasive visualization of blood flow within the heart and blood vessels. Stenotic or regurgitant valves can be assessed at the bedside. Quantitative measures using color flow Doppler methods (the PISA technique) allow accurate measurement of the degree of valvular regurgitation.
- 2-Dimensional echocardiography allows the visual appreciation of cardiovascular anatomy and function.
• Transesophageal echocardiography (TEE), introduced in the late 1980s, revolutionized echocardiography by imaging the heart using an ultrasonographic probe placed in the esophagus. Today TEE is used in outpatient, inpatient, and intraoperative settings and is especially important in the assessment and management of endocarditis, valvular disease, congenital defects, vascular abnormalities, and other problems not well seen from the surface of the body. Cardiac surgery is now routinely monitored with TEE.

• Stress echocardiography (exercise or pharmacologic stress) provides clinical information regarding ischemic potential.

• Contrast echocardiography provides enhanced images at rest or under stress after injection of small amounts of gas into the bloodstream.

• Harmonic imaging is a new means of measuring the vibration of sound waves within the heart. The harmonic image enhances picture quality especially with contrast images and in technically difficult studies.

• The newest advances are 3-dimensional (3-D) and 4-dimensional (4-D) echocardiography (Figure 3). “Instead of a tomographic image of the heart, the whole structure creates a picture—a 3-D or moving 3-D (called 4-D) image—that has an extremely realistic appearance, even to the untrained person,” says James B. Seward, MD, former echocardiography laboratory director at Mayo Clinic in Rochester. These realistic images create an entirely new computer-generated science of structural visualization, quantitation, and mathematical displays of physiology called parametric imaging (Figure 4).

• Ultrasound-tipped catheters provide intravascular and intracardiac real-time imaging.

Landmark achievements of echocardiography are numerous and include the following:

- A 90% reduction in diagnostic cardiac catheterization of children with congenital heart disease and adults with valve disease. Today, hemodynamic evaluation by echo and Doppler techniques has substantially supplanted invasive heart catheterization for the measurement of cardiac function and pressures.

- Echo-directed pericardiocentesis, which historically was associated with high mortality.

- Early diagnosis and management of endocarditis.

- Emergent diagnosis of aortic dissection.

- A marked increase in the safety and completeness of cardiac surgery.

- Early diagnosis of coronary artery disease.

- Confident characterization of cardiac masses and tumors.

- Better understanding of the cardiomyopathies.

Echocardiography has made immense contributions to world health care and has become the most commonly used cardiovascular imaging modality in the United States. Technology has allowed miniaturization, reducing the size of the diagnostic unit from a refrigerator-sized console to hand-held (<5 pounds) and ultimately palm-sized devices. Transducers range from large transthoracic (>20-mm diameter) to transesophageal (7- to 15-mm diameter) to catheter-tipped (2- to 3-mm diameter) and ultimately injectable or implantable devices.

The evolution of ultrasonicographic imaging has been driven by close collaboration among cardiologists, engineers, physicists, and industry. Mayo Clinic has played an integral role in the development and clinical application of echocardiographic technology. According to Fletcher A. Miller, Jr, MD, current director of the echocardiography laboratory, Mayo Clinic physicians and scientists have published thousands of papers related to echocardiography since the first was published by Dr Schattenberg in the Mayo Clinic Proceedings in 1968 and have received more than 25 patents. The Mayo Echo Research Center was recognized by the National Institutes of Health in 2003 as a core clinical research facility. In addition, Mayo Clinic investigators currently are participating in more than 100 echocardiography clinical research trials. In 2003, over 60,000 patients had echocardiographic procedures at Rochester campus and outreach sites. Mayo Clinic continues to collaborate with industry, researchers, and clinicians from around the world to further develop and refine this modality.
Experience, Careful Selection Improve Aortic Valve Repair Outcomes

Treatment of valvular regurgitation has changed markedly over the past 2 decades. This is particularly true for mitral valve regurgitation, in part because of the accuracy of echocardiography in defining the severity and mechanism of valve leakage, a better understanding of the natural history of the disease, and the predictability of repair of degenerative mitral valve disease.

Less progress has been made in treating chronic aortic valve regurgitation, but recent studies suggest that the traditional conservative strategy of deferring valve replacement until there is clear-cut evidence of ventricular dysfunction, progressive left ventricular enlargement, or symptoms may result in excess mortality.

Earlier intervention for aortic valve repair or replacement may prove to be the best strategy for patients who have well-documented severe aortic regurgitation. However, operation for chronic aortic valve regurgitation usually leads to prosthetic replacement, and concerns regarding complications of prostheses only reinforce a conservative clinical approach. Aortic valve repair offers the potential advantages of early intervention, without the potential complications associated with prosthetic valves.

Valve repair has been an accepted approach in patients with acute and chronic aortic dissection, annuloaortic ectasia, and congenital heart disease, but the role of repair for primary aortic valve disease is not well defined. “Our experience suggests that primary aortic valve repair can be performed in selected patients with low risk and excellent freedom from valve-related morbidity and mortality,” says Hartzell V. Schaff, MD, chairman of the division of cardiovascular surgery at Mayo Clinic in Rochester.

Mechanical valve-related complications, including thromboembolism, anticoagulant-related bleeding, and endocarditis, occur at a rate of approximately 5% per patient-year. The rates of thromboembolism and anticoagulant-related bleeding after aortic valve replacement are lower with biological valves, but structural valve deterioration is expected, and normal function beyond 15 years is unlikely for younger patients. Since 1986, 160 patients have undergone primary aortic valve repair at Mayo Clinic in Rochester. These patients can be categorized into 4 groups on the basis of the cause of aortic valve regurgitation: annular dilation (n=63 [39%]); bicuspid valve (n=54 [34%]); cusp prolapse of the tricuspid aortic valve (n=34 [21%]); and cusp perforation (n=9 [6%]).

Annular Dilation

Annular dilation without cusp prolapse or perforation can cause central valve leakage on account of inadequate cusp apposition. Repair is accomplished by placement of 1 or 2 horizontal mattress plication sutures through the aortic wall at each commissure to narrow the angle of the commissures, reduce the circumference of the annulus, and increase the surface area of cuspal coaptation (Figure 1). Care is exercised to avoid excessive narrowing, which may lead to functional aortic stenosis. Soon after repair of severe aortic valve regurgitation, patients often have higher than normal aortic valve gradients because of large left ventricular stroke volume. If there is any question of adequacy of the valve area after plications, the orifice is calibrated with a dilator to confirm adequate annular size.

Bicuspid Valve

In most patients, regurgitation is caused by retraction or prolapse of the conjoint cusp. The most common anatomic finding is a conjoint cusp beneath the right and left coronary sinuses. Valves are repaired by limited triangular resection and suture repair of the median raphe (Figure 2). This maneuver shortens and elevates the free edge of the cusp, permitting apposition with the noncoronary cusp. The extent of the resection from the free edge toward the annulus should be no more than 30% to 50% of the entire length to preserve the dimension of the cusps and to avoid suture of the thinner area of the central cusp. In a few patients with very pliable cusps, prolapse of the conjoint cusp can be corrected by plication without resection. Because some degree of annular dilation almost always accompanies regurgitation of a bicuspid valve, commissural plication is usually combined with cusp repair.

Cusp Prolapse of Tricuspid Aortic Valve

Regurgitation of tricuspid aortic valves may be caused by prolapse of 1 or more cusps, usually with elongation of the
free edge. Several repair techniques have been used, including cusp plication near the commissure, as described by Trusler, and resuspension of the free edge of the cusp.

**Cusp Perforation**

Cusp perforation resulting from infective endocarditis is repaired by patch closure using autologous pericardium secured with interrupted or continuous sutures (Figure 3).

**Concomitant Procedures**

Hypertrophied or calcified nodules of Arantius may prevent complete coaptation. Seven patients in this series additionally underwent cusp shaving to thin the area restoring pliability of the free edge.

Other concomitant procedures have been performed in 98 of the 160 patients undergoing primary aortic valve repair, including mitral valve repair (n=42 [26%]) and coronary artery bypass grafting (n=29 [18%]). One postoperative death occurred, and 2 patients had reoperation during the initial hospitalization. Long-term follow-up has been obtained in 96%; 16 late deaths occurred (Figure 4), and 16 patients had late reoperation for aortic valve replacement (2.8±2.5 years after initial operation).

**Outcomes**

These late results should be interpreted in the context of expected results from prosthetic valve replacement. “Replacement with a mechanical or a biological prosthesis would be expected to have a lower rate of reoperation during the first 5 to 7 years, but this durability comes at the expense of valve-related complications,” says Dr Schaff. As with the early experience with mitral valve repair, aortic valve repair also had a learning curve. Rates of late reoperation have been reduced by half in the latter portion of this group.

Congenital bicuspid aortic valves are present in approximately 2% of the general population, and up to 63% of people with bicuspid aortic valves have no significant valve dysfunction with normal life expectancy. However, valvular regurgitation is a frequent presentation in younger patients, most commonly attributable to prolapse of the conjoint cusp. “These younger patients may be the best candidates for valve repair, with 91% of our patients in this series free from reoperation at 5 years,” says Dr Schaff.

The risk of endocarditis after repair is unknown; it is recommended that clinicians advise their patients to follow guidelines for prophylaxis for subacute bacterial endocarditis. Patients should be evaluated by a cardiologist yearly. “We recommend an echocardiogram at 1 year and thereafter at the discretion of the cardiologist,” says Dr Schaff.
Catheter Ablation for Atrial Fibrillation: A Promising Alternative to Drug Therapy

For the past 3 decades, drug therapy has been the mainstay of treatment for patients with atrial fibrillation (AF). In many patients, that therapy is directed at controlling the ventricular response rate. Membrane-active drugs may be used to restore and maintain sinus rhythm; however, numerous studies have shown that only 40% to 60% of patients treated with classical membrane-active drugs remain in sinus rhythm at the end of 1 year of treatment. Enthusiasm for this level of efficacy is tempered by the constitutional adverse effects, organ toxicity, and proarrhythmic consequences accompanying drug therapy for rhythm control.

“Despite therapy, some patients remain highly symptomatic because of recurrent AF, inadequate rate control, or drug-induced adverse effects,” says Douglas L. Packer, MD, of the Heart Rhythm Service at Mayo Clinic Rochester. “This lack of response to drug treatment has provided the incentive for the development of nonpharmacologic therapies for patients with AF whose symptoms persist despite drug therapy.”

Curative Nonpharmacologic Therapy

Trigger-Mediated AF

One such highly effective strategy has been based on the demonstration that most episodes of paroxysmal AF arise from “trigger” sites within pulmonary veins (PVs). The elimination of this arrhythmia is now possible through electrical isolation of the PVs from the left atrium using catheter ablation techniques (Figure 1). Ablation energy is directed at eliminating the effect of the triggers responsible for initiating AF in patients with predominantly paroxysmal AF in the absence of appreciable underlying heart disease. These patients present with episodes of self-limited AF, frequent atrial premature complexes (APCs), or immediate recurrence of AF after cardioversion. The total electrical isolation of the PVs is also critical, as these foci can be responsible for maintaining AF, in addition to triggering it.

During the procedure, the junction between the vein and the left atrium is ablated using radiofrequency energy through a point-to-point approach. Ablation can also be accomplished by delivering ultrasonographic or laser energy or by freezing PV tissue using cryoablatative approaches. These techniques are now being tested in investigational studies at Mayo Clinic. AF-triggering foci can also arise within the superior cava, posterior left atrium, and vein of Marshall. Between 4% and 11% of patients have demonstrated repetitively firing foci from within these non-PV sites (Figure 2).

“In our experience with more than 400 patients with AF who have undergone ablation since 1998, the source responsible for generating AF can be completely isolated in the majority of patients,” says Dr Packer. “In patients with paroxysmal AF, this translates into the elimination of AF in 70% to 75% of patients throughout 18 months of follow-up.” Furthermore, 10% of patients who continue to have AF respond completely to antiarrhythmic drug therapy, even though this was not the case before ablation.
An additional 10% of patients show a substantial decrease in AF frequency with or without drug therapy. As a result, 90% of patients have a substantial improvement or are cured over a short-term experience of 24 months. The beneficial effect may be augmented by altered atrial conduction or altered parasympathetic stimulation of the heart.

Of interest, AF recurs in between 10% and 20% of patients after ablation, but it then resolves during the first 4 to 6 weeks after treatment. These recurrences may represent a form of proarrhythmia related to the irritation from the ablation intervention.

Substrate-Mediated AF
In other patients, the AF is more dependent on abnormal atrial tissue or “substrate” problems. Patients may have atrial enlargement or scarring or other cellular level abnormalities. In many patients, the increased complexity of substrate-mediated AF requires additional intervention in the form of linear ablation. For patients with new-onset AF, the trigger responsible for initiation of an arrhythmia is of paramount importance in producing paroxysmal symptoms. As the underlying disease or AF progresses, substrate-mediated factors responsible for maintenance of AF become more important, thus leading to persistent or permanent AF (Figure 3). In these patients, a more extensive procedure can be done to ablate a larger area of the posterior left atrium and create linear lesions between the PVs and the mitral valve annulus (Figure 4). This wide-area circumferential ablative approach interrupts electrical activation, thereby decreasing the chance for reentrant activity required for sustaining AF.

To determine the contribution of this approach to AF treatment, we examined the outcome of ablative intervention in 106 patients with persistent and chronic AF. Many of them had underlying heart disease or atrial enlargement. AF was eliminated in 69% of the patients, and 87% were AF free, including those on antiarrhythmic therapy. This outcome compares favorably with that in the control group of patients with AF treated with PV isolation only, in which 45% were without AF, and 67% were controlled with additional antiarrhythmic drug therapy. Although this remains a rapidly evolving practice incorporating advanced mapping and ablation technology, linear ablation, including PV isolation, appears to be effective in selected patients with symptomatic, persistent, or chronic AF associated with more diffuse substrate. This approach may also be effective in patients with underlying heart disease such as dilated or hypertrophic cardiomyopathy producing heart failure.

In The News
Treatment of Asymptomatic Patients With WPW Syndrome, Revisited

Since the emergence of endocardial catheter-based techniques in treating cardiac arrhythmias in the 1980s, radiofrequency ablation of the accessory pathway has become the treatment of choice in patients with symptomatic Wolff-Parkinson-White (WPW) syndrome.

“In asymptomatic patients who do not work in high-risk occupations (eg, pilots, firefighters, and schoolbus drivers), a conservative approach has been generally accepted by experts because of the low rate of spontaneous arrhythmias and the low risk of sudden death,” according to Win-Kuang Shen, MD, from the Mayo Clinic Heart Rhythm Service. This consensus-based practice has been challenged by a recent study from Italy reported in the New England Journal of Medicine.

In this prospective study, asymptomatic patients at “high risk” for arrhythmias (those younger than 35 years with arrhythmias inducible during electrophysiologic testing) were randomly assigned to ablation therapy or observation. During follow-up, the incidence of spontaneous arrhythmias was significantly higher and 1 ventricular fibrillation event occurred.

These findings have renewed the debate on how best to treat asymptomatic patients with WPW syndrome, and a comprehensive review will be presented in an upcoming issue of Cardiovascular Update.

Figure 3. The role of initiation triggers versus maintenance substrate in the pathogenesis of AF. Shown is the relative importance of either factor, as a function of the duration of AF. Early in the clinical course, triggers responsible for the initiation of AF are the most prominent contributor giving rise to paroxysmal or persistent tachycardia. With advanced disease, left atrial enlargement, or prolonged AF, the importance of the substrate for maintenance of the arrhythmia increases substantially, giving rise to difficult, persistent, or permanent AF. (Reprinted with permission of the publisher from Packer DL. Linear ablation for atrial fibrillation: the pendulum swings back. In: Zipes DP, Hausberger M, eds. Catheter Ablation of Arrhythmias, 2nd ed. Armonk, NY: Futura Publishing Co; 2002:107-129.)
Even if the AF is not completely eliminated, a marked improvement in quality of life is observed with ablative intervention. “We have evaluated quality of life in 30 patients in whom ablation failed,” says Dr Packer. “The duration and frequency of AF was reduced in these patients, and fatigue, dyspnea, chest pain, and exercise tolerance were improved compared with the preablation baseline.”

**Risk of AF Ablation**

The success of ablation must be considered within the context of the procedure’s risks. Complications related to the catheterization itself can occur in 1% of patients. Severe bradycardia occurs in 0.5% of patients, and tamponade, stroke or TIA, or phrenic nerve damage occurs in 0.5% to 1% of patients. PV stenosis may occur in 1% to 3% of patients, depending on the procedure undertaken (Figure 5). Overall, major complications occur in 1% to 3% of patients, with less severe events occurring in 5% to 7% of patients undergoing ablation.

**AF Palliation**

In other patients, ablative interventions such as right atrial linear ablation may be used to palliate underlying AF without eliminating it. This procedure typically is reserved for patients with extensive atrial disease with persistent AF or atrial flutter despite left atrial ablation. This approach alone is effective in eliminating AF in 10% of highly selected patients, but it may only reduce the burden of AF in other individuals, particularly when used with adjunctive treatment such as antiarrhythmic drug or device therapies.

**Rationale for Nonpharmacologic Therapy**

The rationale for any nonpharmacologic therapy for AF should be considered carefully. Decreased stroke risk may be a valid reason to proceed with a new procedure. It should be noted, however, that no ablative study has clearly demonstrated a reduction in stroke occurrence. Furthermore, ablative intervention may lead transiently to increased stroke risk after the procedure. Warfarin therapy, in contrast, has been universally demonstrated to provide a significant reduction in the occurrence of stroke or peripheral thromboembolic events. As such, stroke prevention is not currently a clear-cut indication for ablative intervention.

An additional reason for proceeding with nonpharmacologic therapy is to prevent tachycardia-induced cardiomyopathy. Recent data also support the extension of aggressive intervention to those with underlying heart disease and more persistent or chronic AF. In the future, this may become a sizable indication for ablative intervention. “In the absence of overall survival and stroke benefits, the decision to proceed with nonpharmacologic therapy is driven by the desire to relieve the symptoms that significantly alter a patient’s quality of life,” says Dr Packer. “As a result, the best candidates for curative ablation or other interventions are those who have highly symptomatic AF and who are unresponsive to at least 1 membrane-active antiarrhythmic drug.”

Which treatment approach is best depends on the individual patient and the nature of his or her AF. Other therapeutic options, including new drugs, surgical techniques, and pacemaker and defibrillator devices, are currently available in clinical practice or are under investigation and will be discussed in future issues of Cardiovascular Update.
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COSPONSORED BY WAKE FOREST UNIVERSITY SCHOOL OF MEDICINE; INFO: 507-284-0536, echocme@mayo.edu

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Aug 9-11, 2004, Whistler, BC
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Oct 3-6, 2004, Rochester, Minn
Info: 507-284-0536, 507-266-6703, echocme@mayo.edu

ECHOCARDIOGRAPHY FOR THE SONOGRAPHER
Sep 26-28, 2004, Rochester, Minn
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