

CARDIOVASCULAR UPDATE

CLINICAL CARDIOLOGY AND CARDIOVASCULAR SURGERY NEWS



Valvular Heart Diseases: New Approaches Lead to Improved Outcomes



Maurice E. Sarano, MD

The nature of valvular heart disease and its diagnosis and treatment changed dramatically during the past century with the introduction of antibiotics, a better understanding of the pathophysiology of infectious endocarditis, and the development of effective valve repair and replacement techniques. Rheumatic valvular disease is

now uncommon in developed countries. However, the increasing number of older persons (Figure 1) has resulted in a new epidemic of degenerative valvular disease. "Mayo Clinic uses a multidisciplinary team approach to integrate clinical acumen, technical skill, and education to provide comprehensive long-term care to patients with valvular heart disease," says Maurice E. Sarano, MD, director of the Mayo Clinic Valvular Heart Disease Clinic in Rochester.

Diagnostic Modalities

The most common valvular abnormalities seen in developed countries are mitral valve regurgitation and aortic valve stenosis. The decline in surgical morbidity and mortality has led to the concept that some patients should be offered early operation before they develop functional compromise. "Offering patients surgical repair or replacement before they become severely symptomatic requires diagnostic certainty and a complete and accurate description of the lesions to be treated," says Dr Sarano. Numerous diagnostic modalities may be used, depending on the patient's clinical presentation.

Doppler Echocardiography

For patients with valvular stenosis, this technique can be used to measure valve gradients and area; measured results are verified by physicians with extensive imaging experience. For patients with valvular regurgitation, Mayo Clinic has developed and refined new methods such as the PISA (proximal isovelocity surface area) method (Figure 2). The regurgitant blood volume is routinely assessed and the volume overload objectively defined. It is also possible

to measure the effective regurgitant orifice as a reflection of lesion severity and, importantly, to determine whether the lesion is repairable.

Electron Beam Computed Tomography (EBCT)

EBCT is a noninvasive, ultrafast imaging method that can be used in the diagnosis of dilation and hypertrophy of cardiac chambers and the quantification of valvular calcification (Figure 3). This capability is of particular importance for patients with aortic valve stenosis in whom the severity of the stenosis may be otherwise difficult to define.

Magnetic Resonance Imaging (MRI)

MRI is another noninvasive imaging method especially useful in the evaluation of the aorta of patients with connective tissue disease or aortic valve disease (Figure 4) to determine whether replacement with a composite graft is feasible.

Intracardiac Ultrasonography

With this new echocardiographic application, intracardiac images are obtained via an ultrasonographic transducer placed at the tip of a cardiac catheter. It can be useful for patients in whom imaging is difficult, and it complements cardiac catheterization.

Monitoring Techniques

The timing of surgical intervention in patients with valvular disease remains a nagging question for cardiologists and

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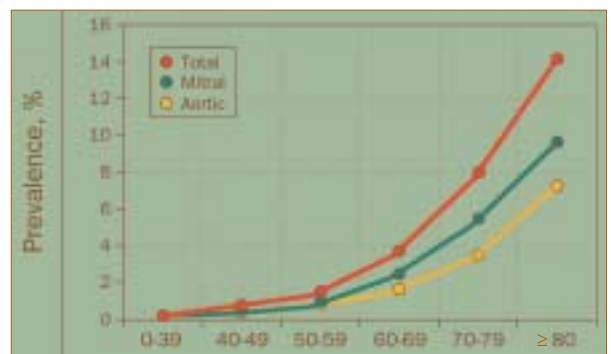


Figure 1. Prevalence of valve diseases by age group in Olmsted County, Minnesota. The marked predominance of valve diseases in older patients foreshadows a new epidemic of valve diseases as the population ages.

surgeons. For patients with known valvular disease, serial Doppler echocardiography continues to be an extremely useful tool for follow-up and monitoring. Recent data from the Valvular Heart Disease Clinic suggest that brain natriuretic peptide activation, a marker of left ventricular failure and remodeling, is also a marker for poor outcome. Another major advance has been the inclusion of cardio-pulmonary exercise testing (CPET) in the evaluation. CPET measures, among other important characteristics, the oxygen consumption with peak exercise and provides an objective measure of exercise capacity. CPET commonly demonstrates that “asymptomatic” patients are limited in their activity. For example, research at Mayo Clinic has shown that approximately 1 in 5 patients with mitral regurgitation who report no symptoms have markedly reduced functional capacity and might be candidates for early intervention. These new tools greatly improve the ability to detect early signs of clinical deterioration.

Treatment

Medical treatment of valve disease has been limited for the most part to palliation of heart failure immediately preceding surgical intervention. A new emphasis on slowing or halting the progression of valve disease has led to the conduct of clinical trials to test the efficacy of medical treatment. Mayo Clinic is currently participating in clinical trials in conjunction with the National Institutes of Health to evaluate the effectiveness of angiotensin blockade and of β -blockade in retarding the progression of mitral regurgitation

and the use of statins in slowing the progression aortic stenosis.

Valve preservation has been attempted for many years, but only recently have repair techniques been developed that produce reliable results. At Mayo Clinic, more than 90% of patients with mitral regurgitation are eligible for valve repair (compared with only 40% of patients nationally). When valve replacement cannot be avoided, newly designed prosthetic valves are available with improved hemodynamic profiles and lower thromboembolic risks. The combined improvements in surgical technique and cardiac anesthesia have greatly decreased operative risks. Now, surgery can be considered earlier in the course of the disease, especially for elderly patients who previously were not considered candidates for surgery.

Balloon mitral valvuloplasty changed the approach to mitral stenosis. Research is ongoing to create new intra-vascular devices that will spare patients the risks and inconvenience of an operation. Clinicians are hopeful that some of these devices will duplicate the successes of balloon valvuloplasty.

The Valvular Heart Disease Clinic brings together the expertise of cardiovascular surgeons, cardiologists, echocardiographers, interventionists, and nursing staff to provide the best possible clinical care. “An important emphasis is placed on educating the patient and family,” says Dr Sarano. “Treatment really is a team approach.”

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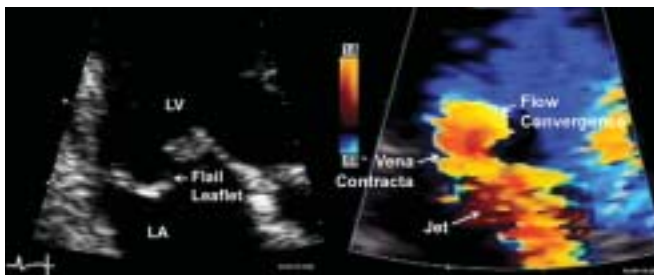


Figure 2. Echocardiographic imaging of a flail mitral valve (left) with the corresponding color-flow imaging of the flow convergence zone (right). This Doppler echocardiographic imaging approach is essential to quantify valve regurgitations. LA, left atrium; LV, left ventricle.

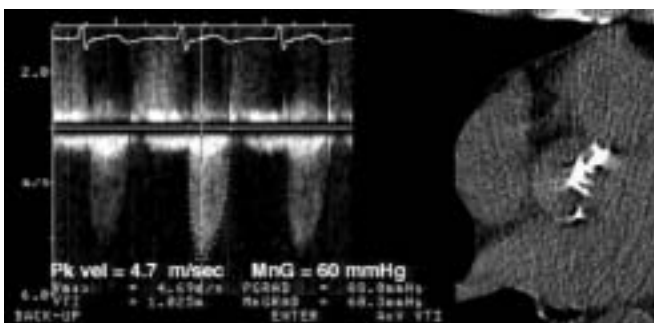


Figure 3. Assessment of severity of aortic stenosis by (left) Doppler echocardiography with measurement of transvalvular blood velocity and mean gradient and (right) EBCT showing the large mass of calcification (white density) accumulated on the aortic valve.

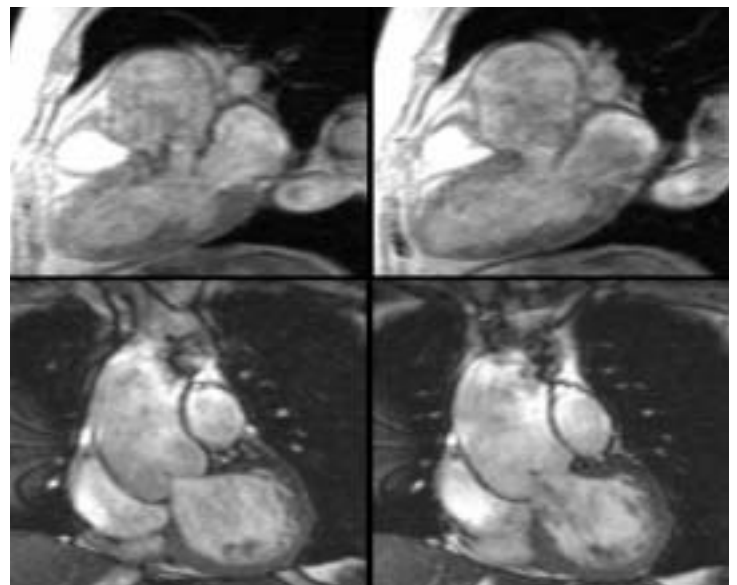


Figure 4. MRI scans of the heart and aorta in a patient with aortic regurgitation due to annuloaortic ectasia.

Coming soon to *Cardiovascular Update's* Web site ...
Clinical Trials in Cardiology and Cardiovascular Surgery

Xenotransplantation Offers Solution to Organ Shortages

Next Few Years May See Bridge, End-Stage Applications



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Approximately 5 million Americans have heart failure, and the incidence is about 400,000 new cases per year. Heart failure is the primary or contributory cause of 260,000 deaths per year. Mortality in patients with advanced New York Heart Association class III or IV heart failure exceeds 50% at 2 years, and that for end-stage class IV patients on both oral and intravenous therapy is 70% at 6 months. Cardiac allotransplantation is the only accepted therapeutic alternative at this time.

More than 60,000 heart transplants have been performed worldwide, and 2,300 are performed annually in the United States. "Outcomes are excellent, with 1-, 5-, and 10-year survivals of 93%, 82.5%, and 67.4%, respectively, at Mayo Clinic in Rochester," according to cardiovascular surgeon Christopher G. A. McGregor, MD, director of the Mayo Clinic William J. von Liebig Transplant Center. "Many patients who receive heart transplants return to active, productive lives, albeit requiring lifelong immunosuppressive therapy." The total need may be as high as 50,000 heart transplants annually; thus, the unmet need is nearly 48,000 transplants. The lack of donors is reflected not only in the unmet need for transplantable hearts, but in the huge discrepancy between the number of patients on the United Network for Organ Sharing (UNOS) waiting list for solid organ transplants (>80,000) compared with the number of transplants actually performed each year (approximately 24,000).

Xenotransplantation: Why Is the Pig Considered the Ideal Donor?

1. Physical size of organs similar to humans
2. Commercially available with established husbandry techniques
3. Short gestation period (4 months)
4. Large litter size
5. Low age of sexual maturity
6. Complement system analogous to humans
7. The pig genome can be genetically engineered
8. The pig can be cloned
9. Zoonoses may be less likely than in primates
10. Can be maintained in a pathogen-free environment
11. Inexpensive to maintain
12. Societally more acceptable

suitable donor is unlikely to be available, however, other solutions such as left ventricular assist devices and artificial heart systems, cellular transplantation, or xenotransplantation will be necessary.

Xenotransplantation

Xenotransplantation is defined as any procedure that involves the transplantation, implantation, or infusion into a human recipient of either (1) live cells, tissues, or organs from a nonhuman animal source or (2) human body fluids, cells, tissues, or organs that have had ex vivo contact with live, nonhuman animal cells, tissues, or organs. The pig is currently considered the potential donor of choice (Table).

Barriers to Transplantation

The major scientific barriers to successful xenotransplantation are potentially infectious (xenozoonosis), immunologic, and physiologic. Disease transmission from animal sources of organs is potentially endogenous and exogenous. The principal endogenous concern arises from the potential of porcine endogenous retrovirus to infect a human recipient. Substantial investigation of this possibility has taken place over the past 5 to 10 years, and evidence to date suggests little risk to humans. Strategies to minimize the risk of exogenous infection from pigs include germ-free cesarean derivation of source animals for the donor herd, use of filtered air, irradiated feed, and chlorinated water for the pigs, and an extensive bacteriologic screening program. To satisfy these requirements (outlined by the US Food and Drug Administration), a unique transgenic pig barrier facility has been constructed in Rochester, Minnesota, to provide future animal donors that would satisfy these stringent infectious disease requirements.

Immunologic barriers include hyperacute, vascular (perhaps cell-mediated), and chronic rejection. Hyperacute rejection is caused by activation of the classical complement pathway by preformed antibody deposition to surface epitopes in other species. Humans and Old World monkeys are unique in that they share such preformed antibodies to the surface epitope of galactose (1,3) galactose (Gal) present in all other species. The engineering of pigs transgenic for human complement-regulating proteins has essentially abolished hyperacute rejection as a barrier in xenotransplantation. The technique of adding human genes to the pig is now well established.

Another barrier to successful xenotransplantation is vascular rejection of the cardiac xenograft with myocardial necrosis and associated microvascular thrombosis. The predominant cause of this vascular rejection is deposition of Gal antibodies on the xenograft. A new drug to control these antibodies has been developed and tested by researchers at Mayo Clinic and its industrial partner. This medication is a specific galactose-containing polymer that not only effectively neutralizes circulating Gal but also controls resynthesis. During the past 7 years, a number of

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studies have been carried out at Mayo Clinic in Rochester exploring different immunosuppressive regimens for cardiac xenotransplantation. The median duration of functioning heterotopic transgenic pig cardiac xenografts has been prolonged now to more than 3 months (Figure). Future strategies to further improve results include the use of Gal knockout pig donors, which will be available soon.

The Challenge and Promise of Clinical Application

The FDA and the International Society for Heart and Lung Transplantation have outlined tentative preclinical animal experimental requirements for consideration of early clinical application. Although no exact recommendations have been made and a range of views has been expressed, a median survival of 3 months in a consecutive series of orthotopic transplants from transgenic pigs to nonhuman primates has emerged as a potential starting point for early clinical trials. This outcome should be achieved in the absence of life-threatening complications from immunosuppressive therapy.

In recent months Mayo Clinic has had substantial initial success with life-sustaining orthotopic cardiac xenografts. These as yet unpublished results offer real promise of clinical applicability within the next few years. Current challenges to clinical application include reliable diagnostic modalities to predict vascular rejection and effective treatments to reverse rejection.

“Initial clinical application of cardiac xenotransplantation will likely be a bridge to

allotransplantation for patients who are poor candidates for ventricular assist devices or for patients who have severe end-stage heart failure and are not transplant candidates,” says Dr McGregor. “While current results do not justify clinical application today, we are clearly moving in the direction of clinical application within a few years.”

The advantages of cardiac xenotransplantation over mechanical devices remain compelling. In particular, the hearts come in all sizes, offer total heart replacement, are totally implantable, and have no need for an extrinsic power source or anticoagulation. Continuing genetic modification of donors promises ever-improving performance, perhaps reducing the need for immunosuppression in the future. The recent success of orthotopic preclinical transplantation at Mayo Clinic offers enormous potential for the future.



Median duration of functioning heterotopically transplanted transgenic pig hearts.

Catheter-Based Closure of Atrial Septal Defect and Patent Foramen Ovale



Guy S. Reeder, MD, Donald J. Hagler, MD

Recent innovations in catheter-based technology now allow closure of defects in the mid portion of the atrial septum, which previously required a surgical approach. “Secundum atrial septal defect (ASD) and patent foramen ovale (PFO) can now in most cases be treated safely with septal occluder devices, obviating the need for surgery,” according to Guy S. Reeder, MD, consultant in the cardiac catheterization laboratory at Mayo Clinic in Rochester.

Secundum Atrial Septal Defect

Patients with isolated ASD are usually asymptomatic until their fourth decade. Untreated, the right ventricular volume overload created by

longstanding left-to-right shunting may lead to pulmonary arterial hypertension and right ventricular failure. Traditionally, a pulmonary-to-systemic flow ratio of 1.5:1.0 suggests that left-to-right shunting is severe enough to warrant surgical closure. A percutaneous approach allows safe closure at the time of diagnosis.

Candidates for device closure include patients with uncomplicated isolated secundum defects with diameters of up to 38 mm. In their deployed configuration, commonly used devices resemble 2 flat buttons with a short connecting waist (Figure 1). The waist diameter is selected to fit the stretched diameter of the ASD. Devices can be delivered through a transeptal sheath and are deployed under fluoroscopic and echocardiographic guidance (Figure 2). “Although

complications such as device embolization, cardiac tamponade, and thrombosis have been recorded, they are distinctly rare," according to Donald J. Hagler, MD, pediatric cardiologist at Mayo Clinic in Rochester. "Device deployment takes only about 40 minutes; patients are observed overnight and dismissed the following day and may resume most normal activity almost immediately."

Success rates of percutaneous closure are similar to open surgical closure, but general anesthesia, cardiopulmonary bypass, and a prolonged recovery period can be avoided. Device closure has an overall lower risk of complications than surgical repair, which will likely make early treatment preferable.

After the procedure, aspirin, 325 mg daily, is prescribed indefinitely, and prophylaxis for infectious endocarditis is recommended for 6 months after device deployment. The risk of thromboembolic complication is less than 1% using this regimen. Because fluoroscopy is used for device placement, women of childbearing age should have a negative pregnancy test before undergoing the procedure. Exclusion criteria include patients with septum primum or sinus venosus ASDs, correctable anomalies of the pulmonary veins, or associated conditions that warrant cardiac surgery.

Patent Foramen Ovale

Indications for closure of PFO are less obvious. The controversy stems from the difficulties determining exactly who is an appropriate candidate for closure. Although patients referred for closure occasionally have evidence of substantial right-to-left shunting, most patients have had cryptogenic stroke, and the PFO is presumed to be a source of paradoxical embolization from the venous system. A PFO can be demonstrated in up to 27% of the "normal" population undergoing echocardiographic or transcranial Doppler examination. Associated

anatomic features thought to increase the risk of paradoxical embolization include large size of the PFO, the presence of a hyper-mobile or aneurysmal fossa ovalis membrane, the presence of a prominent eustachian valve directing inferior vena caval flow toward the fossa ovalis, and a large resting or inducible right-to-left shunt by echocardiographic bubble study.

Although the presence of a PFO with right-to-left shunting seems to be a risk factor for transient ischemic attack (TIA) and stroke, the difficulty in an individual patient is determining whether this finding is related to the patient's stroke or is an unrelated occurrence. Since patients are seen after the fact, the diagnosis of paradoxical embolization remains a presumptive one, after other likely causes are excluded.

"Mayo Clinic in Rochester is participating in randomized trials of device closure versus medical therapy; device closure is offered to selected patients while awaiting results of these trials," says Dr Reeder. These studies include younger patients (often but not always less than 55 years old) with 1 or more well-documented strokes or TIAs and no other explanation from imaging studies and hypercoagulable workup. More than 95% of patients have complete closure at 3 months, and the incidence of device-related complications is extremely low.

In a series of 100 patients who underwent ASD or PFO closure for the indication of stroke or TIA at Mayo Clinic in Rochester, 3 patients had recurrent events during an 18-month follow-up period. Complete closure of the PFO was documented after device placement in all 3 patients, indicating a likely unrelated cause for the neurologic event. Similar results have been reported in patients who underwent surgical closure. "These findings underscore the difficulty in determining the cause of the neurologic event in any individual patient and the need for further studies in this area," says Dr Hagler.

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Figure 1. Septal occluder device in deployed configuration.

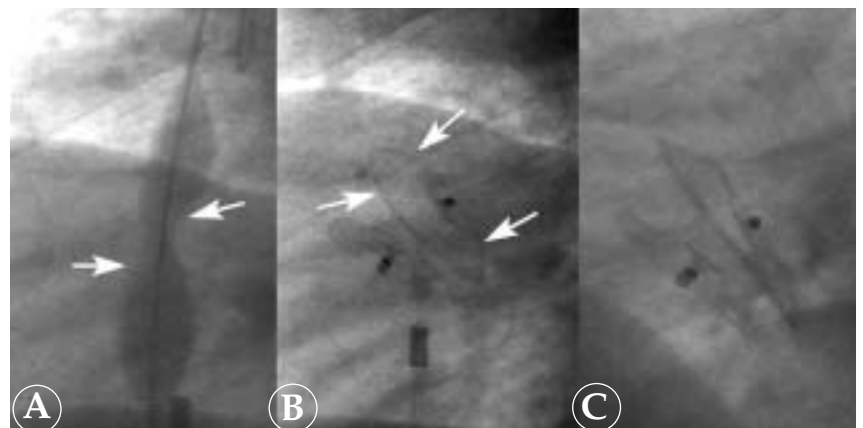


Figure 2. (A) Radiographic image during PFO closure. A low-pressure sizing balloon has been placed across the PFO and inflated. Arrows delineate the left and right atrial sides of the patent foramen. (B) Deployment of a closure device. Arrows delineate the left atrial side of the device in this anteroposterior view. An imaging catheter is seen lower center. (C) Lateral view of deployed device. The left and right atrial sides are clearly seen and surround the atrial septum from each side.

Sleep Apnea Raises Blood Pressure, Heart Disease Risk



Virend K. Somers, MD, PhD, Eric J. Olson, MD

TABLE 1

Clinical Features Suggesting OSA Hypopnea Syndrome

History

Breathing disturbances during sleep

- Loud, disruptive snoring
- Choking/gasping
- Witnessed episodes of apnea

Difficulties maintaining sleep

- Frequent awakenings
- Restless sleep

Daytime dysfunction

- Sleepiness

Physical Examination Findings

Obesity

Obstructing nasal lesion(s)

- Polyps
- Septal deviation
- Turbinate hypertrophy

Crowded oropharynx

- Tonsillar hypertrophy
- Macroglossia
- Low-lying soft palate and uvula

Retrognathia

Thick neck (in men, collar size >17 inches)

Hypertension

Increasingly, sleep apnea is being implicated in the pathophysiology of cardiac and vascular disease. Sleep apnea is either obstructive or central, with some patients having a combination of both types. "Obstructive sleep apnea (OSA) occurs when the upper airway narrows or collapses with inspiration during sleep. The patient undergoes multiple, brief, and repetitive Müller maneuvers (inspiration against a closed upper airway) until the obstruction is overcome, usually because of subclinical arousals," according to Virend K. Somers, MD, PhD, cardiology consultant at Mayo Clinic in Rochester. "Central sleep apnea (CSA), often interchangeably known as Cheyne-Stokes respiration, refers to periodic absence of breathing efforts," he says.

Obstructive Sleep Apnea

Patients with predominant OSA are frequently, although not always, overweight or obese. Obesity and weight loss are recognized as important causes of worsening or attenuation of OSA, respectively. "The periods of apnea are especially marked during rapid eye movement sleep or when patients are sleeping on their backs, and it may also be worsened by alcohol intake before sleep," says Eric J. Olson, MD, co-director of the Mayo Clinic Sleep Disorders Center in Rochester. "The nocturnal hypoxemia in patients with OSA can be very severe, sometimes resulting in oxygen desaturation to levels as low as 40% to 50%." These patients also experience very disturbed sleep and therefore are sleep deprived and may also have daytime somnolence (Table 1).

The repetitive nocturnal desaturation and retention of carbon dioxide may induce serious pathophysiologic responses that carry over into waking hours. Apnea and hypoxemia activate chemoreflexes that induce vasoconstriction and acutely raise nocturnal blood pressure. Hypoxemia also elicits release of endothelin, catecholamines, and other vasoactive substances that may

be associated with longer-term trophic effects on the heart and blood vessels. Additionally, OSA patients may have activation of systemic inflammatory markers, such as C-reactive protein and cytokines. The repetitive blood pressure increases and systemic inflammation may contribute to endothelial dysfunction, thus predisposing to longer-term blood pressure elevation. Even during the day, OSA patients who are normoxic, awake, and breathing normally have very high levels of sympathetic activity and faster heart rates.

The most compelling evidence linking OSA to the development of cardiovascular disease has been demonstrated in patients with hypertension. In long-term follow-up of patients with severe OSA, patients with increasing apnea severity left untreated for 4 years had a strikingly higher risk of developing new hypertension. Treatment of the sleep apnea resulted in lower blood pressure, not only at night but also during the day.

The hemodynamic responses and neurohumoral activation associated with repetitive nocturnal hypoxemia may also have deleterious effects in patients with congestive heart failure (CHF). About 10% of patients with CHF may have serious OSA. This prevalence is likely to be higher in CHF patients who are overweight or obese. "Treatment of OSA in patients with CHF lowers daytime blood pressure and improves ejection fraction and functional capacity," says Dr Somers. "Whether treatment of OSA improves mortality in patients with CHF remains to be determined."

An increased risk of cardiac arrhythmias has also been noted in OSA patients. Several studies have suggested a higher frequency of ventricular premature beats, atrial tachyarrhythmias, or both, although the evidence remains inconclusive. In patients with atrial fibrillation undergoing cardioversion, those with untreated OSA had a 1-year recurrence rate double that of patients with OSA receiving adequate treatment with continuous positive airway pressure (CPAP). The prolonged apneas may also induce serious bradyarrhythmias such as high-grade atrioventricular block or sinus arrest because of activation of the diving reflex. Treatment of OSA typically results in marked improvement or resolution of these bradyarrhythmias in the presence of a normal cardiac electrical conduction system.

Because hemodynamic and hypoxic stress may place an increased burden on ischemic myocardium, OSA has also been implicated in nocturnal angina. Both chest pain and ST depression during sleep are attenuated by treatment of OSA.

Sleep apnea has also been associated with increased risk for cerebrovascular disease. However, no longitudinal data definitively link OSA to increased risk for stroke.

TABLE 2
A Night at the Mayo Clinic Sleep Disorders Center

7 PM: Check-in

8 PM: Application of monitoring equipment

Bedtime: Lights out at the patient's typical bedtime

Diagnostic Study (first half of the sleep study): The goal is to obtain at least 2 hours of diagnostic sleep time on which to determine the extent of the disordered breathing. During this period, the patient is asked to sleep on both back and sides to see how position influences breathing.

Therapeutic Study (second half of the sleep study): CPAP is applied and titrated to the effective level.

Arise Time: Study over at 6 AM

Discussion of Test Results: Patients meet with a consultant from the Sleep Disorders Center on the morning after their overnight test to review the test results and treatment options.

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The standard of care for OSA is CPAP, which uses positive airway pressure to “splint” the airway open during inspiration. Between 30% and 40% of OSA patients may not tolerate CPAP, and alternative or supplementary therapeutic approaches include weight loss, avoidance of supine position while sleeping, and avoidance of alcohol. Although tracheostomy may be a last-resort treatment for life-threatening OSA, particularly in patients with severe cardiovascular disease, other surgical options and dental appliances have been used. More evidence is needed to confirm the efficacy of these interventions. A single report suggests that cardiac pacing may attenuate the severity of sleep apnea in patients with nocturnal bradycardia, although these findings have yet to be confirmed.

Central Sleep Apnea

CSA affects about 40% of patients with CHF and has been linked to poorer prognosis in these patients. The mechanisms that elicit CSA in patients with CHF are not fully understood, although factors such as increased ventilatory

sensitivity to carbon dioxide, pulmonary congestion, increased cardiac filling pressures, and delayed circulatory time may be involved. CSA in patients with heart failure has been linked to arrhythmias, including ventricular premature beats and atrial fibrillation. CHF patients with CSA have higher levels of plasma and urine norepinephrine. “Whether CSA and poorer outcome in patients with CHF occur because CSA is an epiphenomenon of more severe CHF or because CSA activates pathophysiologic mechanisms in and of itself remains unclear,” says Dr Olson. However, even patients with asymptomatic left ventricular dysfunction have a high prevalence of CSA. Furthermore, recent studies suggest that treatment of CSA in patients with CHF may improve 5-year transplant-free survival.

Treatment of CSA in CHF patients is challenging, because many of these patients do not tolerate CPAP. Aggressive treatment of the CHF itself, with afterload reduction and decreased cardiac filling pressures, may greatly improve CSA.

The association of repetitive nocturnal apneas with cardiovascular disease provides an opportunity for a potentially important and novel therapeutic strategy: treatment of sleep apnea may help limit cardiac disease progression and attenuate severity. “Sleep apnea should be considered in patients with cardiovascular disease that is poorly responsive to conventional treatment, such as resistant hypertension, intractable heart failure, and recurrent atrial fibrillation,” says Dr Somers. The epidemic of obesity suggests that OSA may play an increasingly important role in cardiac and vascular disease in future years.

The Mayo Clinic Sleep Disorders Center provides comprehensive evaluation and treatment for patients with sleep disorders (Table 2). “Recognition and aggressive treatment of sleep apnea are important components of overall cardiac care,” says Dr Somers.



2004 American College of Cardiology highlights (left to right): Raymond J. Gibbons, MD, Stephen C. Hammill, MD, Bijoy K. Khandheria, MD, Sudhir S. Kushwaha, MD, and David R. Holmes, Jr, MD, were all members of the 2004 ACC Scientific Sessions Program Committee. Additionally, Dr Gibbons was awarded the ACC 2004 Distinguished Fellow Award, and Dr Holmes was appointed to the ACC Board of Trustees. Dr Hammill is the 2004 president of NASPE/Heart Rhythm Society. Dr Khandheria is the 2004 ASE vice president.

Upcoming Courses

CONTINUING MEDICAL EDUCATION, MAYO CLINIC

Heart Failure: Standard and Advanced Management Strategies

May 18, 2004, Rochester, Minn
Info: 800-533-1710, 507-266-3074

Perspectives in Women's Health: Heart Failure in Women [interactive satellite program]

May 20, 2004, Rochester, Minn
Info: 866-869-4069, womenshealth@mayo.edu, www.mayo.edu/womenshealth

Valvular Heart Disease 2004: New Strategies for the Third Millennium

Jun 10-12, 2004, Rochester, Minn
Info: 800-288-6296, 507-266-0677, cvcme@mayo.edu

9th Annual Mountain Course: Success With Failure: New Strategies for the Evaluation and Treatment of Congestive Heart Failure

Aug 8-10, 2004, Whistler, British Columbia
Info: 800-323-2688, 507-284-2509, cme@mayo.edu

Echo Alaska: Integration of Echo Findings in Clinical Decision Making

Aug 15-22, 2004, aboard *Sapphire Princess*
Cosponsored by the American Society of Echocardiography
Info: 507-284-0536, echocme@mayo.edu

Internal Medicine Review for Nurse Practitioners and Physician Assistants

Sep 16-17, 2004, Rochester, Minn
Info: 800-323-2688, 507-284-2509, cme@mayo.edu

Perspectives in Women's Health: Sleep Disorders in Women [interactive satellite program]

Sep 23, 2004, Rochester, Minn
Info: 866-869-4069, womenshealth@mayo.edu, www.mayo.edu/womenshealth

20th Annual Echocardiography in Congenital Heart Disease

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
Info: 800-288-6296, 507-266-0677, cvcme@mayo.edu

Cardiovascular Board Review and Recertification

Oct 2-7, 2004, Rochester, Minn
Info: cme@mayo.edu, www.mayo.edu/cardiologyreview

AMERICAN COLLEGE OF CARDIOLOGY PROGRAMS

To register or for information about programs, visit www.acc.org or call the ACC Resource Center at 800-253-4636, ext 694. Outside the United States and Canada, call 301-897-2694 or fax request to 301-897-9745. Additional contact information, when available, is listed for individual courses.

18th Annual Echocardiographic Workshop on 2-D and Doppler Echocardiography at Vail

Jul 25-29, 2004, Vail, Colo
Directed by: George M. Gura, MD, FACC; Fletcher A. Miller, MD, FACC; Jae K. Oh, MD, FACC

Cases in Echocardiography: TEE, Doppler, and Stress: Interpretation and Clinical Decision Making for the Advanced Echocardiographer

Oct 28-30, 2004, Seattle, Wash
Directed by: Rick A. Nishimura, MD, FACC; Fletcher A. Miller, Jr, MD, FACC



Mayo Clinic cardiologist Sharonne N. Hayes, MD, speaks at the White House Health Truth Event in the East Room on February 2, 2004. Dr Hayes joined President Bush and First Lady Laura Bush at the event to kick off American Heart Month. (White House photo by Susan Sterner)



OTHER EDUCATION OPPORTUNITIES

Update in Hospital Medicine

May 13-15, 2004, Rochester, Minn
Info: 800-323-2688, 507-284-2509, cme@mayo.edu

Mayo Clinic Nicotine Dependence Conference

May 16-19 and Oct 24-27, 2004, Rochester, Minn
Info: 800-323-2688, 507-284-2509, cme@mayo.edu

Current Issues in Clinical Research

Aug 26-27, 2004, Rochester, Minn
Info: 800-533-1710, 507-266-3074

Genomics in Clinical Practice: What You and Your Patients Need to Know

Oct 11-12, 2004, Rochester, Minn
Info: 800-323-2688, 507-284-2509, cme@mayo.edu

Mayo Clinic CARDIOVASCULAR UPDATE

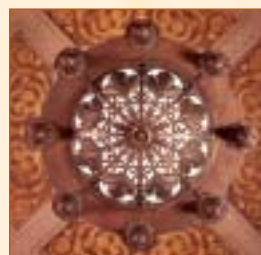
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Ceiling detail of Plummer Building, Mayo Clinic, Rochester, Minnesota.