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# CARDIOVASCULAR UPDATE



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David J. Bradley, MD, PhD

In January 2005, indications for implantable cardioverter-defibrillators (ICDs) were subbroadened stantially include most to patients with a left ventricular ejection fraction (EF) of 35% or less. This change translates into a 2- to 3-fold increase in the number of Medicare beneficiaries eligible for ICDs. Expanded

indications for ICDs are largely the result of 2 recently published randomized trials, the Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT) and the Comparison of Medical Therapy, Pacing, and Defibrillation in Chronic Heart Failure (COMPANION) trial.

#### **Primary vs Secondary Prevention ICDs**

From the time of their initial clinical use in 1980, ICDs have been indicated for cardiac arrest survivors. In this secondary prevention role, ICDs shock or pace the heart out of recurrent ventricular arrhythmias and reduce all-cause mortality by about one-third. "Cardiac arrest survivors, however, make up only a small minority of the hundreds of thousands of patients who experience ventricular arrhythmias annually in the United States," says David J. Bradley, MD, PhD, an electrophysiologist at Mayo Clinic in Rochester. "Most patients at high risk for lethal arrhythmias have no history of cardiac arrest but do have a left ventricular EF less than 35%." Extending the use of ICDs from secondary to primary prevention of arrhythmic death has been the subject of several trials in recent years.

The largest primary prevention ICD trial, SCD-HeFT, was reported in the *New England Journal of Medicine* in January 2005. In this trial, 2,521 patients with mild to moderate heart failure symptoms (New York Heart Association class II or III), a left ventricular EF of 35% or less,

and no history of cardiac arrest were randomly assigned to ICD placement versus antiarrhythmic drug treatment with amiodarone versus placebo. Importantly, SCD-HeFT included a sizable number of patients with nonischemic heart failure, a group that had not previously been shown to benefit from primary prevention conventional ICD therapy. After a median follow-up of 45 months, patients who received ICDs had a statistically significant 23% relative reduction in all-cause mortality versus placebo. Antiarrhythmic drug therapy showed no survival benefit. SCD-HeFT is remarkable because it showed convincingly that primary prevention ICD placement in a broad population of heart failure patients saves lives. By using straightforward inclusion criteria (EF≤35% and mild to moderate heart failure symptoms), SCD-HeFT has also helped simplify patient selection for ICD placement. "Largely gone is the need to risk-stratify patients with invasive electrophysiologic studies before proceeding to ICD placement," says Dr Bradley.

Primary prevention ICD placement is also performed in some patients with an EF higher than 35%. This may occur, for example, in patients with a combination of coronary artery disease, nonsustained ventricular tachycardia, an EF between 36% and 40%, and inducible ventricular arrhythmias. Other patients with an EF higher than 35% considered for ICD placement include selected patients with long QT syndrome, congenital heart disease, hypertrophic cardiomyopathy, syncope, or arrhythmogenic right ventricular dysplasia.

## New-Generation ICDs Improve Quality of Life

Although conventional ICDs, like those used in SCD-HeFT, reduce mortality, they generally do not improve quality of life. A new generation of ICDs, termed "cardiac resynchronization therapy-defibrillators" (CRT-Ds), has been developed to address the limitations of conventional ICDs. Unlike conventional ICDs that pace only the right side of the heart, CRT-Ds have an additional pacing lead that allows

## Conventional ICDs versus Newer-Generation ICDs (CTR-Ds)

CHARACTERISTICS	CONVENTIONAL ICD	NEWER-GENERATION ICD (CRT-D)
Benefits		
Survival	Yes	Yes
Quality of life	No	Yes
Patient eligibility		
Ejection fraction	Variable	<35%
Heart failure symptoms	Variable	Moderate to severe
ECG QRS duration	Any	>120 ms
Implantation		
INR at time of implantation	<2.6	<1.6
Procedure time	About 1 h	About 2-4 h
Number of leads	1-2	2-3
Hospital stay	1 d	1 d
30-d Mortality in trials	About 1%	About 1%-2%
Device function		
Defibrillation	Yes	Yes
Bradycardia pacing	Yes	Yes
Antitachycardia pacing	Yes	Yes
Cardiac resynchronization	No	Yes

CRT-D, cardiac resynchronization therapy-defibrillator; ICD, implantable cardioverter-defibrillator; INR, international normalized ratio.

Heart Rhythm Services

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Pediatric Cardiology

them to pace both ventricles. With this simultaneous ventricular pacing, CRT-Ds correct the underlying dyssynchronous ventricular contraction common in failing hearts. Whether this cardiac resynchronization therapy and the resulting improvement in cardiac pumping ability result in better quality of life was studied in the COMPANION trial.

In COMPANION, 903 patients with advanced heart failure (New York Heart Association class III or IV), a depressed left ventricular EF of 35% or less, and left ventricular dyssynchrony (left bundle branch block) were randomly assigned to CRT-D versus medical therapy. After a median follow-up of 16 months, patients who received CRT-Ds had a statistically significant 36% relative reduction in all-cause mortality versus medical therapy alone. CRT-D patients in COMPANION also had better quality of life and exercise capacity. COMPANION showed for the first time that ICDs could improve survival and quality of life in selected patients.

Use of CRT-Ds has increased dramatically because of their ability to improve quality of life as well as survival. CRT-Ds will likely account for half of all ICDs implanted in the United States this year, versus 5% or less in 2001. Ongoing research in advanced cardiac imaging may help extend the use of CRT-Ds even further. Currently, CRT-Ds are generally indicated only for patients who remain highly symptomatic from heart failure despite treatment with proven heart failure medications, including angiotensin-converting enzyme inhibitors and  $\beta$ -blockers. (CRT pacemaker-only devices also are available. These devices are used infrequently in the United States, however, because virtually all patients eligible for CRT pacemaker-only devices are also eligible for CRT-Ds.)

## **Conventional ICDs versus Newer-Generation ICDs (CRT-Ds)**

The table compares conventional ICDs and CRT-Ds. Both increase survival, but only CRT-Ds improve quality of life. Generally, patient eligibility is less restrictive and implantation is simpler for conventional ICDs. Conventional ICD implantation usually can be performed in patients who are taking warfarin, whereas warfarin is temporarily withdrawn before CRT-D implantation. Length of hospital stay after implantation is typically 1 day for patients receiving either type of device. Thirty-day mortality (based on recent randomized trials) is approximately 1% for conventional ICDs and 1.8% for CRT-Ds. These mortality figures are not unexpected given the severity of the patients underlying heart disease, and they are less than a nationally representative 5.4% 30-day mortality rate for comparable patients undergoing coronary artery bypass graft surgery. Both conventional ICDs and CRT-Ds are capable of defibrillation, bradycardia pacing, and antitachycardia pacing. Only CRT-Ds increase the pumping ability of the heart via cardiac resynchronization therapy.

## Contraindications

Primary prevention ICD placement is generally deferred in patients who have had an acute myocardial infarction (MI) within the previous 40 days or coronary artery stenting or surgical bypass within the preceding 3 months. This delay gives the patient s EF time to improve after MI or revascularization, thereby obviating the need for an ICD. ICDs are generally not implanted in patients with reversible causes of ventricular arrhythmias, projected survival of less than 1 year from noncardiac disease, or irreversible brain damage. "Despite their ability to improve survival and quality of life, ICDs are probably underutilized in the United States," says Dr Bradley. "Less than 25% of eligible patients are thought to undergo ICD placement nationally."

The Mayo Clinic Heart Rhythm Service welcomes the opportunity to counsel patients about the merits of implantable defibrillators.

## A Systems Approach to Surgical Excellence



Douglas A. Wiegmann, PhD

#### Cardiovascular Surgery

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A marker of surgical excellence is the ability to successfully manage unexpected events during surgery. However, even experienced surgical teams can be stalled by minor problems that disrupt surgical flow. For example, one of the few published studies of its kind observed pediatric cardiothoracic surgeons performing neonatal arterial switch operations. The study found that, on average, 7 adverse events occurred per procedure, with most events arising from errors made by the surgical team. However, few of these events were life-threatening (major events). Most were relatively minor events that disrupted the surgical flow but did not immediately jeopardize the safety of the patient. "None-

theless, as the number of minor events increased, the likelihood that the surgical team was able to cope with a major event decreased," says Douglas A. Wiegmann, PhD, a National Institutes of Health Clinical Research Scholar in the Division of Cardiovascular Surgery at Mayo Clinic in Rochester. "Minor events seemed to cumulatively erode the limited compensatory resources of the surgical team in this study."

This valuable insight highlights the importance of event and error management skills. However, a general review of the literature revealed that no published study has yet analyzed the types of events in



the operating room that actually affect surgical performance. Therefore, little is known about the frequency and nature of surgical flow disruptions, making the development of interventions that effectively improve patient safety even more challenging. Without effective interventions, errors with serious consequences continue to occur at a high rate in many surgical specialties, including cardiac surgery, vascular surgery, and neurosurgery.

Research in other complex settings (eg, aviation) suggests that human error is often caused by myriad active and latent factors, probably the least of which is an unsafe act by an individual. Therefore, interventions that target underlying systemic factors may be more effective than approaches that focus exclusively on individual characteristics. As illustrated in the flowchart, a systems approach to understanding errors would consider the skill of the surgeon and the condition of the patient, as well as

- environmental factors—equipment design and/ or environmental distractions;
- social factors-teamwork and communication;
- supervisory issues—training, staffing, and scheduling; and
- organizational variables—procedures, policies, and resources.

According to this perspective, errors are the natural consequences (not the causes) of a systemic breakdown among the factors that affect performance. As a result, patient safety programs are likely to be most effective when they intervene at specific failure points within the system or render the system more tolerant to the occurrence of such failures (ie, increase the ability of the surgical team to manage events when they occur).

The systems perspective is relatively new to medical practice. Historically, the culture within most health care settings has been one of placing blame for errors solely on individuals. However, the systems approach to understanding surgical errors is becoming more widely accepted within many surgical specialties. "Refinements in surgical skill may be a relatively small component in reducing surgical morbidity and mortality," says Dr Wiegmann. Optimizing details in equipment design, communication, team organization, and decision making may be as important as refining surgical skill to achieve optimal patient outcome.

Unfortunately, the growing acceptance of the systems perspective in surgical practice has not translated into similar development and growth of effective error prevention and patient safety programs. This situation may be due, at least in part, to the fact that

many safety programs are developed without a full understanding of the underlying systemic problems that actually cause surgical errors. Furthermore, many patient safety initiatives have been modeled after programs used in other high-risk industries, with the assumption that the systemic error-causing factors in other industries parallel those in health care. For example, teamwork training programs that have proven effective in aviation are being applied in the surgical domain to improve patient safety despite a lack of empirical data concerning the frequency and nature of these issues as causes of surgical flow disruptions or their relationship to surgical errors. This failure to apply an evidence-based approach to teamwork training has prevented most surgical specialties from embracing these programs and has limited their impact on patient safety in the operating room.

Anecdotal and sentinel event reports suggest that teamwork and communication may be vital to patient safety. However, empirical research into real-time dynamics of teamwork and communication in surgery is still at a very early stage. Additionally, other factors such as environmental distractions, equipment design, or resource availability may be equal (if not more important) contributors to surgical errors. At least 1 study suggests that teamwork and communication may contribute less to causing surgical errors than they do in impacting a surgeon s ability to cope with extraneous disruptions or manage errors when they do occur. Consequently, if teamwork training or any other type of patient safety program is to be effective, it must be based on empirical data concerning the actual nature and frequency of surgical flow disruptions that affect performance and error management processes.

"At Mayo Clinic in Rochester, we are launching a research program to help remedy this situation by prospectively studying surgical flow disruptions and their relationship to surgical errors in the context of cardiovascular surgery," says Dr Wiegmann. As part of this project, digital audiovisual recordings of cardiovascular surgical cases will be collected and systematically reviewed by an interdisciplinary team of surgical and human factors experts to identify empirically the frequency and nature of surgical flow disruptions and their effect on surgical performance and error management processes of surgical teams. The results of this project will provide a foundation for developing specific data-driven intervention strategies and the necessary methods and measurement tools to validate the impact of future safety programs, such as teamworking training or preoperative briefings. "We plan to disseminate our findings in future issues of Cardiovascular Update so that everyone can learn from the outcome of this endeavor," says Dr Wiegmann. "After all, surgical excellence is best achieved by learning from both the successes and mistakes of others."

Please see the *Cardiovascular Update* Web site for links to published studies on system analysis.

**Questions for Cardiovascular Update** 



### **Estrogen Therapy and Cardiovascular Disease**

More information from the Women's Health Initiative suggests that younger menopausal women, between the ages of 50 and 59 years, may receive cardiac protection from estrogen therapy, but older women do not derive these same benefits. The report emphasized that hormone therapy (HT) should not be used expressly to prevent heart disease, but these findings may reassure younger women experiencing moderate to severe hot flashes or other menopausal symptoms that HT may be an option for them.

"These new findings are consistent with earlier and ongoing observational studies," says Sharon L. Mulvagh, MD, a cardiologist at Mayo Clinic in Rochester. Andrew E. Good, MD, a gynecologist at Mayo Clinic in Rochester agrees: "These data emphasize the need for additional research to test the hypothesis that estrogen may be good early and bad late in a younger group of recently menopausal women." Both Mulvagh and Good are coinvestigators on the Kronos Early Estrogen Prevention Study (KEEPS).

"KEEPS is designed to provide useful new data to address ongoing questions women have about the utility of hormone treatments and to help guide future research and patient care," says Virginia M. Miller, PhD, principal investigator for KEEPS at Mayo Clinic in Rochester. Seven other study centers are also participating in KEEPS. This 4-year multicenter study is a randomized, controlled, double-blind trial of 720 women, designed to provide prospective data on the risks and benefits of HT in recently menopausal women, particularly as it relates to the progression of atherosclerosis through changes in carotid intimal thickening and coronary calcification. Each center is recruiting 90 women who have not had a hysterectomy and who have been menopausal for less than 3 years. For more information about KEEPS, visit www.keepstudy.org or call 866-878-1221.

# **Apical Ballooning Syndrome: A Mimic of Acute Myocardial Infarction**



Abhiram Prasad, MD

Cardiac Catheterization, Therapeutics, and Interventional Cardiology Laboratory

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The association between stress and cardiovascular symptoms has been recognized for a long time. Cardiologists at Mayo Clinic in Rochester have become aware of a well-defined clinical syndrome, originally described in the Japanese population and termed "takotsubo cardiomyopathy," after a Japanese word for an octopus trapping pot with a round bottom and narrow neck, which resembles the left ventriculogram during systole in these patients (Figure). Other terms used to de-

scribe the condition are "ampulla cardiomyopathy," "broken heart syndrome," and "apical ballooning syndrome" (ABS).

"The precise incidence of ABS is unknown, but it is relatively uncommon and may account for 1% to 3% of patients presenting with an acute coronary syndrome," says Abhiram Prasad, MD, cardiologist in the Cardiac Catheterization, Therapeutics, and Interventional Cardiology Laboratory at Mayo Clinic in Rochester. "It is characterized by transient regional systolic dysfunction involving the left ventricular apex and mid ventricle with hyperkinesis of the basal left ventricular segments. ABS appears to occur almost exclusively in postmenopausal women, although a few cases have been reported in younger women and in men."

The majority of patients have a clinical presentation indistinguishable from an acute coronary syndrome. Most present with chest pain at rest, although some patients have dyspnea alone as the initial presenting symptom. A few patients may present with syncope or, rarely, with out-of-hospital cardiac arrest. The patients are usually hemodynamically stable, although clinical findings of mild to moderate congestive heart failure commonly coexist. In a minority of patients, hypotension may occur, and this can occasionally be caused by dynamic left ventricular outflow tract obstruction and rarely by cardiogenic shock. A unique feature of ABS is the occurrence of a preceding emotional or physical stressful event in about two-thirds of patients. Importantly, such a trigger may not be observed in all individuals, and its absence does not exclude the diagnosis. We have proposed criteria for making a clinical diagnosis of ABS, and all 4 criteria must be met to establish the diagnosis (Table).

The most common finding on the admission ECG is ST-segment elevation, occurring in approximately 80% of patients. Typically 1 to 2 mm of ST-segment elevation is seen in the precordial leads. Characteristic evolutionary changes that occur over 2 to 3 days include resolution of the ST-segment elevation and subsequent development of diffuse and often deep Twave inversion that involves most leads. New pathologic Q-waves may be seen occasionally, and there is frequent prolongation of the corrected QT interval. Most patients have a small, early increase in cardiac biomarkers, especially when cardiac troponins are measured. The diagnosis frequently is made in the cardiac catheterization laboratory because most patients are initially suspected of having an acute coronary syndrome and are referred for coronary angiography. Patients with ABS, typically, do not have obstructive coronary artery disease. The left ventriculogram shows characteristic regional wall motion abnormalities involving the apical and mid segments and a distribution beyond any single coronary artery with sparing of the basal systolic function.

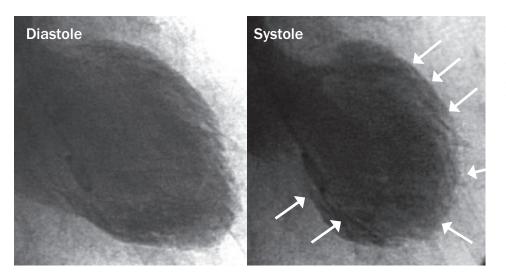
Optimal management of ABS is unknown. Be-

## Mayo Clinic Criteria for the Clinical Diagnosis of Apical Ballooning Syndrome

- Transient akinesis or dyskinesis of the left ventricular apical and midventricular segments, with regional wall motion abnormalities extending beyond a single epicardial vascular distribution
- Absence of obstructive coronary disease or angiographic evidence of acute plaque rupture
- 3. New electrocardiographic abnormalities (STsegment elevation, T-wave inversion, or both)

4. Absence of

- recent severe head trauma
- intracranial bleeding
- pheochromocytoma
- myocarditis
- hypertrophic cardiomyopathy



Left ventriculogram in the right anterior oblique projection during diastole and systole. The mid ventricle and apex are akinetic (arrows), while the basal segments are hyperdynamic, giving the appearance of "apical ballooning" during systole.

IN THE NEWS

cause the presentation of these patients is indistin- $\underline{\aleph}$  guishable from an acute coronary syndrome, initial management should be directed toward treatment of myocardial ischemia with continuous ECG monitoring and administration of aspirin, intravenous heparin, and  $\beta$ -blockers. The syndrome should be suspected in patients with characteristic left ventricular wall motion abnormalities in the absence of obvious

plaque rupture, coronary thrombosis, and occlusive coronary artery disease. Once the diagnosis of ABS has been made, aspirin can be discontinued unless coronary atherosclerosis also coexists.  $\beta$ -Blocker therapy may be continued, if tolerated, especially because an excess of catecholamines may play a role in precipitating the conditions. The precise duration for which  $\beta$ -blocker therapy is required is unknown. Diuretics are effective for the treatment of congestive heart failure. Rarely, when hypotension is extreme, it is important to exclude dynamic left ventricular outflow tract obstruction. Also rare is cardiogenic shock, which is treated with standard therapies, including inotropes and intra-aortic balloon counterpulsation. Anticoagulation

should be considered in cases of severe left ventricular systolic dysfunction to prevent thromboembolism until systolic function recovers.

"Patients with ABS generally have a good prognosis in the absence of severe underlying comorbid conditions," says Dr Prasad. Systolic dysfunction and regional wall motion abnormalities are transient and nearly always resolve completely within a matter of

## **Dietary Fat and Cardiovascular Risk**

Does lowering total fat in the diet lead to a reduction in cardiovascular disease events? No, according to data acquired as part of the Women's Health Initiative (WHI), recently reported in *JAMA*. This trial in postmenopausal women found that a low-fat diet, when compared with a "usual diet," did not result in a reduction of cardiovascular disease events after a 6-year follow-up period.

Reasons for these findings include 1) a modest effect of the intervention diet on lowering cardiovascular risk factors and 2) an unhealthy, greater reduction of "healthy fats" in the intervention group than in the control group.

Adherence to dietary recommendations did not appear to make a difference in outcomes, but study participants who reached the lowest levels of saturated and *trans* fat intake and those with the highest levels of fruit, vegetable, protein, and unsaturated fat intake were generally at lower risk for cardiovascular disease events.

"The study's results are consistent with a growing body of evidence that nutrition-based therapy for cardiovascular disease prevention needs to include a plant-based diet that is rich in carbohydrates, proteins, and healthy unsaturated fats," says Randal J. Thomas, MD, director of the Cardiovascular Health Clinic at Mayo Clinic in Rochester.

Dr Thomas points out the following important factors to consider:

1. Results of the study are consistent with findings over the past 2 decades that the type of fat (saturated, *trans*, monounsaturated, and polyunsaturated fats) may be of more importance in preventing cardiovascular disease than is the amount of fat in one's diet.

2. The WHI trial was primarily designed to test the hypothesis that a low-fat diet would decrease the risk of breast and colorectal cancer in postmenopausal women. The diet used in the trial was, therefore, aimed at limiting all types of fat in the diet, including the "bad fats" (saturated and *trans* fats), as well as the "good fats" (monounsaturated and polyunsaturated fats).

3. There is strong evidence that current dietary guidelines (including ample intake of healthy proteins and fats) decrease cardiovascular risk, particularly in individuals with preexisting coronary artery disease. The WHI dietary trial found that there was actually a trend toward increased cardiovascular disease risk among women with preexisting cardiovascular disease, probably because of the significant reduction in unsaturated fats in the diet.

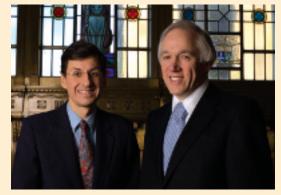
4. The dietary regimen in the WHI trial is not representative of current dietary guidelines for the prevention of cardiovascular disease.

"Current guidelines include recommendations for a plant-based, high-fiber diet that is rich in fruits, vegetables, whole grains, healthy proteins (such as nuts, beans, and low-fat dairy products) and foods that have ample 'healthy fats' (such as fish, olive oil, and canola oil) and limit 'bad fats' (saturated and *trans* fats)," says Dr Thomas. The WHI dietary recommendations were to decrease total fat in the diet to less than 20% of calories by increasing intake of fruits, vegetables, and whole grains. The WHI diet did not encourage the use of healthy proteins or healthy fats.

days to a few weeks. Typically, assessment of the ejection fraction should be performed at 4 to 6 weeks after discharge from the hospital. At this time, the ECG typically demonstrates complete resolution. Inhospital mortality from ABS is very low and unlikely to be higher than 1% to 2%. ABS may recur, although the exact frequency remains to be established. In the Mayo Clinic practice, long-term  $\beta$ -blocker therapy is recommended for most patients. Annual clinical follow-up is advisable because the natural history of ABS is yet to be established.

The underlying pathophysiology of ABS is unknown. Several mechanisms have been proposed, including multivessel epicardial spasm, coronary microvascular spasm, and catecholamine-induced myocardial stunning. Multivessel epicardial coronary artery spasm has not been observed. Microvascular dysfunction is likely to be present in a considerable number of patients, but it remains to be established whether this is the primary mechanism for the injury or a secondary phenomenon. Catecholamines may play a role in triggering the syndrome in view of the fact that many patients have coexisting emotional or physical triggers, and elevated levels of plasma catecholamines have been reported. Important questions remain unanswered: Why does ABS appear to occur almost exclusively in postmenopausal women? Why is there sparing of the basal segments of the heart with characteristic dysfunction of the apical and mid segments? Why is the recurrence rate relatively low? Why does only a very small proportion of the population appear to be at risk for this condition?

Several studies are under way at Mayo Clinic to evaluate the pathophysiology of ABS to address these questions. The investigations involve genotyping, and assessment of coronary microvascular function, echocardiographic features, responses to mental stress, and cardiac sympathetic activity of patients with ABS. An ABS registry has also been established to determine the natural history. Patients wishing to enroll in the research studies or the registry can be referred to the Mayo Chest Pain Clinic after hospital discharge. Mayo Clinic offers a consultative service for patients with a definite or suspected diagnosis of ABS. Physicians may also contact a cardiologist at Mayo Clinic in Rochester by calling 507-284-MAYO for advice on hospitalized patients suspected of having ABS. For more information, please see the Cardiovascular Update Web site.



Raul Emilio Espinosa, MD, has received the 2005 Mayo Clinic Rochester Department of Medicine Laureate Award. Raymond J. Gibbons, MD, is the 2006 president of the American Heart Association.



Win-Kuang Shen, MD, and Paul A. Friedman, MD, are members of the 2006 Heart Rhythm Society scientific program committee.



Rick A. Nishimura, MD, has received the 2006 American College of Cardiology Gifted Teacher Award. Dr Nishimura has also been named to the College Board of Trustees.



David R. Holmes, Jr, MD, has received the 2006 American College of Cardiology Distinguished Scientist Award.

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# **Upcoming Courses**

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Success With Failure: New Strategies for the Evaluation and Treatment of Congestive Heart Failure Aug 6-8, 2006, Whistler, BC Phone: 507-284-6732

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Sep 16-18, 2006, Rochester, Minn

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Sep 17-22, 2006, Rochester, Minn

Mayo Clinic Nutrition in Health and Disease Sep 28-29, 2006, Minneapolis, Minn

See My Heart: Cardiovascular Ultrasound Acquisition and Application Sep 21-24, 2006, Orlando, Fla

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Jul 31-Aug 3, 2006, Vail, Colo Phone: 507-266-6703 or 507-284-0536; fax: 507-266-7403; e-mail: echocme@mayo.edu

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Heart Rhythm Society 27th Annual Meeting May 17-20, 2006, Boston, Mass Phone: 202-464-3400; Web site: www.HRSonline.org

Current Issues in Clinical Research: Latest Trends in Clinical Research Oct 4-6, 2006, Minneapolis, Minn Phone: 800-541-5810



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#### Mayo Clinic Cardiovascular Update

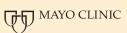
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