MAYO CLINIC

volume 3
number 1
2005

CARDIOVASCULAR UPDATE

CLINICAL CARDIOLOGY AND CARDIOVASCULAR SURGERY NEWS

Early Repair of Coarctation of the Aorta Improves Hypertension Control

Roger F. J. Shepherd, MD
Francisco J. Puga, MD

Periductal coarctation of the aorta can be defined as a discrete area of stenosis of the aorta at or near the point of insertion of the ligamentum arteriosum. This anomaly is believed to result from abnormal involution of ductal tissue during the neonatal period. This form of aortic obstruction is different from the infantile or preductal form, which is associated with other complex forms of congenital heart disease such as hypoplastic left heart syndrome or interrupted aortic arch. Periductal coarctation of the aorta is often associated with bicuspid aortic valve, ventricular septal defect, and/or aneurysmal dilation of the ascending aorta. Periductal coarctation of the aorta may be a component of the Shone syndrome, a rare constellation of obstructive anomalies of the left heart, including congenital mitral stenosis and subaortic stenosis.

"Coarctation of the aorta presenting during the neonatal period or early infancy may cause congestive heart failure, a clinical presentation that demands early and immediate surgical correction," according to Francisco J. Puga, MD, cardiovascular surgeon at Mayo Clinic in Rochester. "In older children and adults, coarctation of the aorta results in upper extremity and cephalic arterial hypertension and may be complicated by cerebral hemorrhage and abnormalities of the ascending aorta, including aneurysmal dilation and aortic dissection and rupture." Roger F. J. Shepherd, MD, from the Mayo Clinic divisions of hypertension and nephrology and cardiology agrees. "Eighty percent of patients with unrepaired coarctation die before the age of 50 because of one of these complications of arterial hypertension," he says.

Several theories may explain the pathogenesis of hypertension associated with aortic coarctation, including the high resistance to left ventricular outflow or perhaps the resetting of carotid and aortic arch baroreceptors. The most likely mechanism of hypertension in aortic coarctation is now believed to be activation of the renin-angiotensin-aldosterone (RAS) system (analogous to the 1-clip Goldblatt model of renovascular hypertension). Aortic coarctation results in hypertension proximal to the coarctation, but decreased arterial pressure distal to the coarctation. The kidney juxtaglomerular apparatus senses the decreased renal perfusion pressure and in response increases renin synthesis, resulting in the increased generation of angiotensin I. Angiotensin I is converted to angiotensin II by angiotensin-converting enzyme (ACE) present in the lung and on vascular endothelial cells. Angiotensin II is a potent vasoconstrictor increasing peripheral vascular resistance and in addition acts on the adrenal gland to increase aldosterone production resulting in retention of salt and water. Other changes that occur include inactivation of bradykinin and vascular endothelial dysfunction with increased production of endothelin causing further vasoconstriction and elevation in blood pressure.

Coarctation of the aorta must be considered in children and young adults with decreased or absent femoral arterial pulses. It can be confirmed by demonstrating a difference in arterial pressure between the upper and lower extremities. "While there are other causes of dampened femoral pulses, this finding in children and young adults is characteristic of aortic coarctation," says Dr Puga. In patients with long-established coarctation of the aorta, perfusion of the aorta distal to the stenosis occurs via intercostal collateral arteries. The subclavian and internal mammary arteries constitute the source of blood flow to the intercostal arteries and then to the aorta distal to the coarctation. Such collateral circulation is sufficient to maintain the distal circulation but not enough to prevent the development of proximal hypertension. In small infants, the lack of adequate collateral circulation results in congestive heart failure when the degree of aortic obstruction is severe.

Inside This Issue

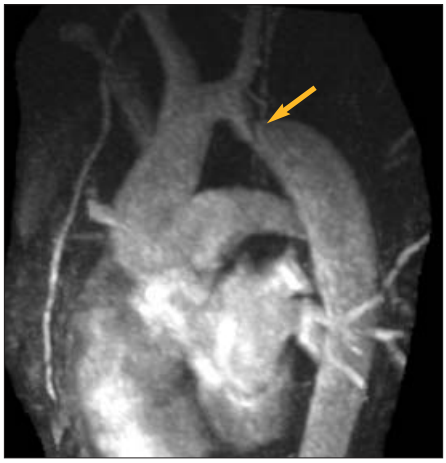


Figure 1. Magnetic resonance image of a typical periductal coarctation of the aorta (arrow).

Confirmation of the diagnosis and further anatomic delineation can be obtained by 1 or more imaging modalities. Aortography, performed by injecting a contrast agent into the ascending aorta and visualizing its course through the aortic arch and descending aorta, provides definitive information about the area and the extent of aortic narrowing and of the degree and efficacy of the collateral circulation. Nevertheless, other less invasive techniques have become the imaging methods of choice. Two-dimensional echocardiography can be very effective in diagnosing and mapping the coarctation area, particularly in infants and small children. Magnetic resonance imaging or computed tomography can provide superb images of the entire aorta, the area of coarctation, and the collateral circulation. These techniques allow impressive 3-dimensional reconstructions of the affected area of the aorta that can help the surgeon in the planning of the reconstructive surgical procedure (Figure 1).

The conventional treatment of coarctation of the aorta in children and adults is surgical. The standard preferred method is resection of the stenotic segment and end-to-end anastomosis. In neonates and infants, adequate resection demands removal of all ductal tissue that may contribute to recoarctation (Figure 2). Other surgical techniques used in the past, such as subclavian flap or prosthetic patch aortoplasty, have been largely replaced by extended resection and end-to-end anastomosis. In adults with fully mature aortas, resection with interposition of a Dacron tube graft may be necessary because the aortic ends lack elasticity and mobility after removal of the stenotic segment.

Surgical repair of coarctation of the aorta has a very low risk of mortality or severe morbidity. Operative complications include hemorrhage from uncontrolled injury to dilated, aneurysmal collateral arteries, recurrent nerve injury, chylothorax from injury to the thoracic duct, and spinal cord ischemia resulting in paraparesis or paraplegia. Of these, the most feared is paraplegia. Risk factors for spinal cord injury include prolonged cross-clamp time, inadequate collateral circulation, anomalous origin of the right subclavian artery, and operation for recoarctation of the aorta. To prevent this disastrous complication, certain precautions must be observed, including minimizing cross-clamp time, topical cooling of the thoracic spinal cord, and using temporary bypass in selected cases.

Complex forms of aortic coarctation in infants and small children are those associated with hypoplastic aortic arch and other cardiac malformations. “Repair of long areas of aortic obstruction requires extensive aortic arch patch aortoplasty using extracorporeal circulation and deep hypothermic circulatory arrest,” says Dr Puga. This same technique can be used to repair recoarctation of the aorta resulting from scarring or lack of growth of the original repair. Additional cardiac lesions can also be addressed using this approach.

In adults with recoarctation or with calcification of the aortic tissues near the area of obstruction, extra-anatomic repair is necessary. Bypassing the obstructed area by interposing a Dacron tube graft between the ascending and descending aortas using a median sternotomy approach and cardiopulmonary bypass is a relatively simple and effective technique (Figure 3). This approach allows for other concomitant procedures (such as aortic valve replacement and coronary revascularization) if needed.

In recent years, percutaneous endoluminal interventions (dilation, stenting, or both) have been used in the treatment of coarctation of the aorta. In infants, percutaneous balloon dilation of the native coarctation can be effective in eliminating the obstruction and is the initial procedure of choice in some centers. Balloon dilation of the native coarctation results in disruption of the aortic intimae, resulting in weakening of the aortic wall and the possible development of false aneurysms. Consequently, Mayo Clinic surgeons have

Cardiovascular Surgery Consultants

Hartzell V. Schaff, MD, Chair
Richard C. Daly, MD
Joseph A. Dearani, MD
Christopher G.A. McGregor, MD
Charles J. Mullany, MD
Thomas A. Orszulak, MD
Francisco J. Puga, MD
Thoralf M. Sundt III, MD
Kenton J. Zehr, MD

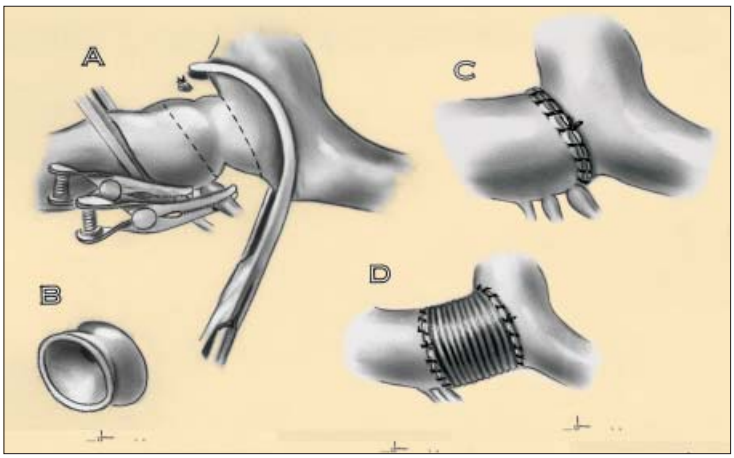


Figure 2. Surgical treatment of coarctation of the aorta. A, Aorta cross-clamped proximal and distal to the coarctation. B, Excised, stenosed segment of the aorta. C, Reconstruction by end-to-end anastomosis. D, Graft interposition.

preferred to treat native coarctation with surgical resection and anastomosis. In adults with native coarctation of the aorta, dilation and endoluminal stenting have been tried with some success. Although disruption of the aortic wall also occurs in this age group, the stent is believed to be helpful in stabilizing the aortic wall injury. Endoluminal stenting is not used when anatomic interference with arterial flow to the aortic arch may occur. Mayo Clinic surgeons have generally preferred the surgical approach because of this risk.

Interventional catheter techniques have been favored in the management of recoarctation of the aorta resulting from scarring or lack of growth of the aortic anastomosis. "In these patients, the potential for serious injury to the aortic wall is less, and successful percutaneous intervention may obviate the need for a difficult operative repair," says Dr Puga.

Division of Nephrology and Hypertension Consultants

Vicente E. Torres, MD, PhD, Division Chair
Gary L. Schwartz, MD, Hypertension Section Head
Vincent J. Canzanello, MD
Vesna D. Garovic, MD
John W. Graves, MD
Eddie L. Greene, MD
James R. Gregoire, MD
Luis A. Juncos, MD
Lilach O. Lerman, MD, PhD
Juan C. Romero, MD
Roger F. J. Shepherd, MD
Clarence Shub, MD
Virend Somers, MD, PhD
Sandra J. Taler, MD
Stephen C. Textor, MD
Stephen T. Turner, MD
Richard M. Weinshilboum, MD
Prince K. Zachariah, MD, PhD

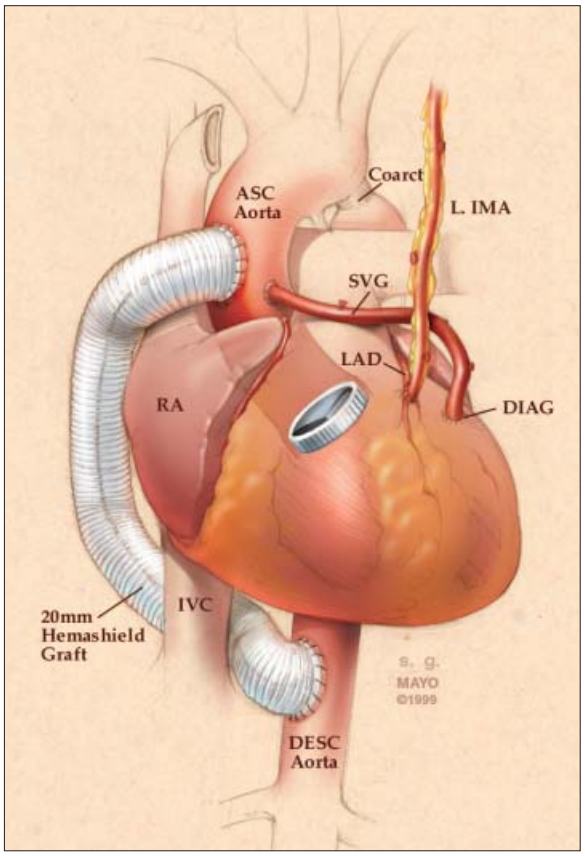


Figure 3. Extra-anatomic reconstruction of aortic coarctation with graft from the ascending to descending aorta. Concomitant aortic valve replacement and coronary revacularization. ASC, ascending; Coarct, coartation; DESC, descending; DIAG, diagonal artery; IVC, inferior vena cava; LAD, left anterior descending artery; L.IMA, left internal mammary artery; RA, right atrium; SVG, saphenous vein graft.

Diagnosed and repaired early in life, aortic coarctation is a potentially curable cause of hypertension. When coarctation is repaired later in life, hypertension tends to be "fixed" on account of structural vessel abnormalities. The cause of this postrepair hypertension is uncertain; however, studies in patients with aortic coarctation have shown a relative deficiency of nitric oxide and greater arterial vasoconstrictor response to noradrenaline, in addition to increased collagen causing stiffer vessels. Timing of the repair is therefore most important. "When aortic repair is performed in patients younger than 5 years, blood pressure normalizes in up to 80% to 90% of them," says Dr Shepherd. "When coarctation is repaired later in life, for example, in teenagers or adults, two-thirds of patients may have persistent chronic hypertension despite successful surgical repair with no residual pressure gradient."

Three types of hypertension associated with coarctation of the aorta:

1. *Preoperative hypertension* associated with long-standing aortic coarctation is primarily due to activation of the RAS system. As a result, elevated blood pressure may respond best to ACE inhibitors or angiotensin-receptor blockers. Other effective medications include β-blockers, which may decrease renin release from the kidney, and diuretics, which counteract the volume and sodium excess associated with sustained hypertension.

2. *Postoperative hypertension* is common immediately after surgery and is usually caused by activation of the sympathetic nervous system. Prophylactic β-blocker medication, begun preoperatively, is recommended.

3. *Chronic postrepair hypertension* can persist despite successful repair. With time, initial changes, including elevated renin, revert to normal. The expanded fluid and blood volume maintains elevated blood pressure, and the RAS system contributes less to chronic elevation in blood pressure. Chronic postrepair hypertension can be treated with standard antihypertensive medications (β-blockers, diuretics, calcium channel blockers, ACE inhibitors, or angiotensin-receptor blockers), recognizing that many patients may require combination therapy with more than 1 antihypertensive medication to reach goal blood pressure.

EECP: Proven Angina Relief, Uncertain Mechanism

Gregory W. Barsness, MD

The growing population of patients with coronary artery disease includes an increasing number who do not obtain acceptable relief of anginal symptoms with conventional therapy. Enhanced external counterpulsation (EECP) is one of the recent novel approaches (including transmyocardial laser revascularization, therapeutic angiogenesis, percutaneous coronary artery bypass, and spinal cord stimulation) being evaluated for the relief of chronic angina. Typically these treatment methods are considered for patients in whom medical management does not adequately control symptoms, or because of previous procedures, unsuitable anatomy, or comorbid conditions, they are not good candidates for interventional or surgical treatment.

EECP has been used in the treatment of angina for the past 2 decades, with a record of safety and a more recent body of literature supporting the technique's efficacy. "It augments diastolic pressure, increases coronary perfusion pressure, and provides left ventricular unloading in a manner analogous to the intra-aortic balloon pump," says Gregory W. Barsness, MD, an interventional cardiologist from the Chest Pain and Coronary Physiology Clinic at Mayo Clinic in Rochester. "It is approved by the Food and Drug Administration for the treatment of chronic or unstable angina and is being evaluated for use in patients with congestive heart failure."

Patients typically receive 35 EECP treatments of 1 hour each over a 7-week period. The device produces an acute hemodynamic effect via 3 sets of cuffs on the upper thigh, lower thigh, and calf of each leg (Figure 1). These cuffs are inflated sequentially with compressed air during diastole and deflated in early systole, raising diastolic aortic pressure, increasing perfusion pressure in the coronary and other arterial beds, and providing mild afterload reduction and increased venous return with a subsequent increase in cardiac output (Figure 2).

Although the mechanism of benefit is unclear, EECP may produce both peripheral and central cardiovascular effects. "Small studies have demonstrated increased levels of growth factors and nitric oxide, as well as improved endothelial function after treatment," says Dr Barsness. "Other potential mechanisms include develop-

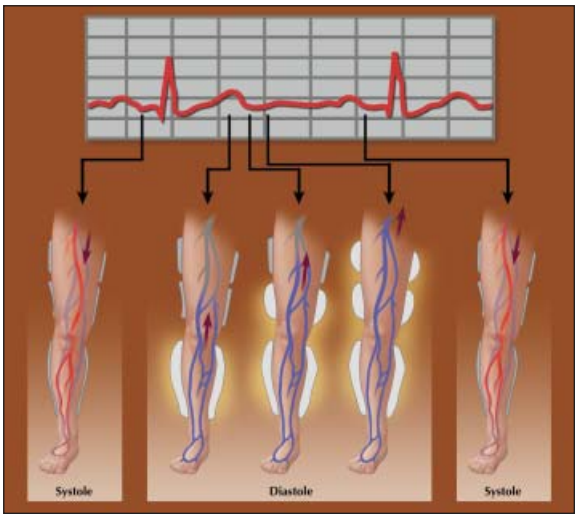


Figure 1. The mechanism of action of EECP. The cuffs compress sequentially during systole and relax at the onset of diastole.

IN THE NEWS

Reports of Late Thromboses Emphasize Importance of Continuing Antiplatelet Therapy After Drug-Eluting Stent Implantation

Since commercial release in 2003, drug-eluting stents have been rapidly adopted as the preferred technology for percutaneous revascularization. Randomized clinical trials have demonstrated the safety and efficacy of drug-eluting stents in reducing the incidence of restenosis and the need for repeat procedures. The initial enthusiasm, however, was tempered by 2 adverse event advisories issued by the US Food and Drug Administration, drawing attention to reports of stent thrombosis occurring within 30 days of deployment. The importance of good deployment technique and dual antiplatelet therapy was emphasized.

Recently, a new concern over late thrombosis was raised. Four cases of late (>1 year) stent thrombosis occurring after discontinuation of all antiplatelet therapy were reported in the October 23, 2004, issue of *The Lancet*. All 4 patients were on long-term antiplatelet therapy with aspirin and were doing well until aspirin was discontinued. In 3 patients, aspirin was discontinued to allow noncardiac endoscopic or surgical procedures. The stents were successfully reopened, but the patients had myocardial infarctions. While the exact reason for these late thromboses remains unknown, it may be related to delayed healing of the artery and incomplete endothelialization of the stents.

"These cases reemphasize the need for indefinite antiplatelet therapy in patients treated with drug-eluting stents," according to Charanjit S. Rihal, MD, director of the Cardiac Catheterization Laboratory at Mayo Clinic in Rochester. Currently, dual antiplatelet therapy with aspirin and clopidogrel is recommended for a minimum of 3 months after implantation of a sirolimus-eluting stent (Cypher stent, Cordis Corporation, Miami Lakes, Florida) and for a minimum of 6 months after implantation of a paclitaxel-eluting stent (Taxus stent, Boston Scientific, Maple Grove, Minnesota). Indefinite therapy with aspirin (81-325 mg daily) is recommended for all patients. "Care should be taken never to discontinue aspirin unless absolutely necessary in the judgment of the patient's physician," says Dr Rihal. "Patients should be counseled never to stop taking aspirin of their own accord and always to check with their physician before making changes in any of their medications."

For more information see the Mayo Clinic *Cardiovascular Update* Web site.

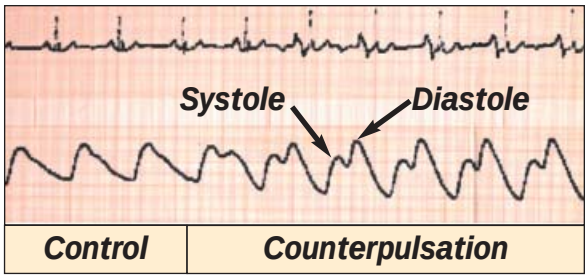


Figure 2. ECG tracing (top) and simultaneous central arterial pressure tracing (bottom). Compression is triggered by the onset of diastole. Diastolic arterial pressure is augmented with counterpulsation compared with that without counterpulsation.

ment of collateral vessels or improved collateral flow via improved diastolic coronary perfusion pressure, alterations in coronary vasomotor tone via neurohormonal mechanisms, or other nonspecific effects of ventricular unloading and improvement in the ratio of oxygen supply to demand."

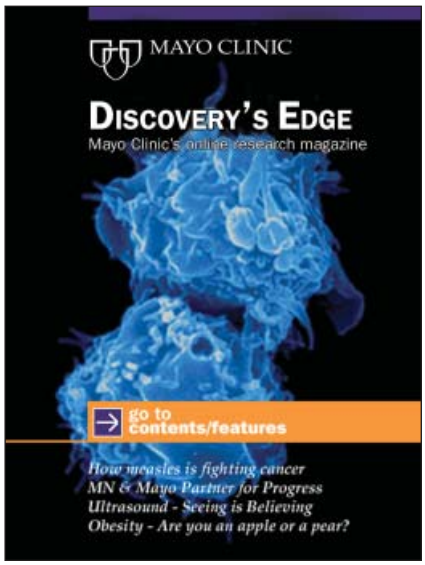
Treatment has also been associated with improved exercise tolerance and myocardial perfusion, as evidenced by both SPECT and PET modalities. The MUST-EECP trial demonstrated a statistically significant increase in time to ST-segment depression with exercise in a group of 56 patients treated with active counterpulsation compared with a sham-treated group. The International EECP Patient Registry has more than 5,000 patients enrolled; more than 80% have improved by at least 1 Canadian Cardiovascular Society angina class, and almost half have improved by more than 2 classes. The benefit has persisted for up to 3 years in this ongoing study.

Contraindications include severe bleeding or thrombotic dyscrasias, pregnancy, severe lower extremity vasoocclusive disease, surgical aortic aneurysm, and any arrhythmia interfering with the ECG trigger. EECP should be used cautiously in patients with severe, uncontrolled hypertension, tachycardia, valvular heart disease, or less severe peripheral vascular disease. Patients need to be cautioned that they may actually have more fatigue during the first weeks after initiating treatment. Medical treatment needs to be optimized, and patients need to continue following diet and exercise recommendations. While EECP provides benefit in decreasing anginal symptoms and permitting increased activity levels, the clinical impact of this approach on myocardial preservation and improved survival have not been demonstrated.

Mayo Clinic in Rochester opened the first EECP center in the upper Midwest in 1999. Originally the primary focus was on research, including small prospective trials and participation in databases. Increasing data supporting the clinical efficacy and safety of EECP, the increasing number of patients who may benefit from this treatment, and Medicare approval for EECP reimbursement have resulted in strong demand for this novel treatment. "We are hopeful that ongoing research will determine in more detail the mechanism of action and verify the long-term attenuation of symptoms with this therapy," says Dr Barsness. "These patients have limited treatment options, and EECP is a safe strategy that provides important symptomatic relief in the majority of patients treated."

Chest Pain and Coronary Physiology Clinic Consultants

Amir Lerman, MD, Director
Gregory W. Barsness, MD
Noel M. Caplice, MD, DrPH
Panithaya Chareonthaitawee, MD
Bernard J. Gersh, MD
David R. Holmes, Jr, MD
Kyle W. Klarich, MD
Abhiram Prasad, MD
Guy S. Reeder, MD
Gurpreet S. Sandhu, MD, PhD
Robert D. Simari, MD
R. Thomas Tilbury, MD
R. Scott Wright, MD



Discovery's Edge **is Mayo Clinic's new online research magazine, featuring stories of Mayo Clinic scientists and physician-researchers and their ongoing research efforts. Learn about population-based research, advances in technology, basic science research, and clinical trials, all at the forefront of medicine. Visit *Discovery's Edge* at discoverysedge.mayo.edu.**

IN THE NEWS

Mayo Clinic Study Demonstrates Yearly Prescription Costs Almost $700 Higher for Obese Patients

Obese patients spend twice as much on prescription drugs as those who are overweight, and nearly 4 times what normal-weight patients spend, according to findings of a Mayo Clinic study presented at the 2004 American Heart Association's Scientific Sessions.

The Mayo Clinic study involved 328 men undergoing comprehensive physical examinations. Their average age was 47 years. They were grouped into the customary categories of normal weight, with body mass index (BMI, weight in kilograms divided by the square of height in meters) of less than 25 kg/m^2; overweight, with BMI of 25 kg/m^2 up to 30 kg/m^2; and obese, with BMI of 30 kg/m^2 or higher. Patients with known cardiovascular disease or serious noncardiac disease were not included. (A table of BMI categories at various heights is available at www.mayoclinic.org/news2004-rst/2501.html.)

Prescription drug costs for the 52 normal-weight individuals averaged $22.84 per month, but the 172 who were overweight spent a monthly average of $39.27. The monthly pharmacy charges for the 104 obese patients averaged $80.31. All major heart risk factors except smoking increased progressively with weight class, as did the prevalence of 6 other medical conditions, including low back pain or degenerative joint disease, erectile dysfunction, sleep apnea, gastroesophageal reflux disease, depression, and gout.

"Costs of illness attributable to overweight and obesity are estimated to be more than $130 billion per year," says Mayo Clinic cardiovascular rehabilitation specialist Thomas G. Allison, PhD, the lead author of the study. "Our study provides just a snapshot of how obesity increases the economic burden for individuals and those who pay for their medical care. For pharmacy costs alone, that extra burden is nearly $700 per individual per year compared with normal-weight individuals."

Troponins Trump CK-MB in Prognostic Value: Fewer False Positives, But Still Need Careful Interpretation

Allan S. Jaffe, MD

For many years, creatine kinase (CK) and its isoenzyme, CK-MB, were used as markers of acute myocardial injury. These markers posed many analytical difficulties, including the potential for false-positive values. The advent of troponin markers for detection of myocardial injury, although a marked improvement, has raised new issues about sensitivity and specificity. Mayo Clinic cardiologist Allan S. Jaffe, MD, a member of the staff of the Cardiac Critical Care Unit and the Department of Laboratory Medicine and Pathology, discusses the use of troponin markers in clinical practice.

1. Are troponin elevations totally specific for the heart? Why are troponins more sensitive than CK-MB?

The present data strongly support the idea that what is measured by the various assays for cardiac troponin I and cardiac troponin T—cTnI and cTnT—comes from cardiac injury. No documented cases of release from other tissues have been reported. Although cTnI and cTnT are different proteins, using high-quality assays, the results for both provide equivalent information, except in patients with renal failure.

For reasons that probably relate to the way in which the fragments are degraded, levels of cTnT are much more frequently elevated in patients with renal failure. Several studies have now confirmed that such elevations identify patients at high risk for subsequent cardiac events.

Troponin is a more sensitive marker than CK-MB because myocytes have much more troponin. In addition, a greater percentage of troponin released from the heart reaches the blood stream because of degradation of CK-MB in myocardium and lymph.

2. Does troponin release always mean myocyte death?

There is legitimate controversy about this issue. It is believed that most troponin elevations that persist are attributable to cell death and release of troponin bound to the myocardial contractile apparatus. In some situations, only transient release occurs (eg, in pulmonary embolism), which could be caused by the release of free troponin protein in the myocyte. In theory, such release could be due to cell death or reversible injury; however, there is no way to distinguish between these mechanisms. Thus, the best term to use when troponin or another other marker is elevated is "cardiac injury."

3. How do I know which assay the lab should use?

Often such decisions are constrained by economics. Regardless, clinicians need to understand the characteristics of the assay used by their clinical laboratory and how the levels that are recommended as cutoff values have been determined.

4. What values are key?

One of the problems in this area is that clinicians and laboratorians have not spoken the same language on this important issue. Each assay has its own structure of values. However, each assay has 3 definable characteristics:

- The *receiver operating characteristic curve* value equates troponin values and those used previously to define

IN THE NEWS

Safety and Efficacy of Cardiovascular Drugs Questioned

Recent reports in scientific and lay publications have raised questions about the use of rosuvastatin (Crestor), one of the relatively new statin drugs prescribed for lipid management, as well as questions about the role of vitamin E in the prevention of cardiovascular disease.

"Rosuvastatin has come under increased scrutiny about its safety record and rate of adverse effects," according to Randal J. Thomas, MD, director of the Cardiovascular Health Clinic at Mayo Clinic in Rochester. Although the use of rosuvastatin may be indicated in some patients, he recommends that rosuvastatin be considered for use only in persons who have high blood cholesterol levels that require medical therapy to lower risk of heart disease and who meet at least 1 of the following 2 criteria:

1. The patient has been found to be intolerant of other statin medications that have well-documented, long-term records of effectiveness and safety (including lovastatin, pravastatin, simvastatin, fluvastatin, and atorvastatin).
2. The patient has not had a satisfactory response to other statin medications.

When rosuvastatin is used, he recommends that patients be monitored closely for the development of adverse effects (eg, muscle soreness, nausea). Patients starting on any statin therapy should have liver enzyme levels checked at baseline, within 6 to 8 weeks of starting therapy, and every 12 months thereafter if earlier findings were stable and within normal limits. Any patient developing musculoskeletal pain should have an evaluation that includes measuring creatine kinase levels.

Research studies performed several years ago suggested that vitamin E may reduce the risk of cardiovascular disease, but several more rigorous research studies done recently have found no clear benefit from its use in preventing heart disease. Data from a recent meta-analysis suggest vitamin E may increase health risk, particularly in high doses (400 IU/d or higher). "As a result of the preponderance of published evidence on this topic, we do not recommend the use of vitamin E for the prevention or treatment of cardiovascular disease," says Dr Thomas.

Elevations of Troponins Without Overt Ischemic Heart Disease

Data suggest that troponin elevation is useful prognostically in patients with

- Congestive heart failure—acute and chronic
- Aortic valve disease and hypertrophic obstructive cardiomyopathy with severe left ventricular hypertrophy
- Postoperative noncardiac surgery patients who seem to do well
- Renal failure
- Critical illness, especially those with diabetes, respiratory failure
- Drug toxicity, eg, doxorubicin, fluorouracil, trastuzumab, snake venoms
- After apparently uncomplicated percutaneous intervention
- Pulmonary embolism, severe pulmonary hypertension
- Sepsis
- Burns, especially if total body surface area >30%
- Amyloidosis
- Acute neurologic disease, including cerebrovascular accident, subarachnoid hemorrhage

No data to suggest troponin elevation is useful prognostically in patients with

- Critical illness, especially hemolytic uremic syndrome
- Infiltrative diseases, such as hemochromatosis, sarcoidosis, and scleroderma
- Trauma (contusion, ablation, pacing, defibrillation/cardioversion, endomyocardial biopsy, cardiac surgery, interventional closure of atrial septal defect)
- Hypertension
- Hypotension
- Severe asthma
- Hypothyroidism
- Coronary vasospasm, including apical ballooning syndrome
- Inflammatory diseases, eg, myocarditis (parvovirus B19), Kawasaki disease, sarcoidosis, smallpox vaccination, myocardial extension of bacterial endocarditis
- Rhabdomyolysis with cardiac injury
- Transplant vasculopathy

Cardiac Critical Care Unit Consultants

Malcolm R. Bell, MD, Director
Gregory W. Barsness, MD
Patricia J. Best, MD
Krishnaswamy Chandrasekaran, MD
Ian P. Clements, MD
Bernard J. Gersh, MD, PhD
Allan S. Jaffe, MD
Andre C. Lapeyre III, MD
Joseph G. Murphy, MD
Jae K. Oh, MD
Abhiram Prasad, MD
Charanjit S. Rihal, MD
Lawrence J. Sinak, MD
R. Thomas Tilbury, MD
Henry H. Ting, MD
R. Scott Wright, MD

acute myocardial infarction with CK-MB. The troponin value has similar (not necessarily identical) sensitivity.

- The *99th percentile* of a putatively normal population. Any value above this is considered abnormal. Unfortunately, at the very low levels of troponins typically seen, there often is a great deal of imprecision in the measurement, so false positives may occur.
- The *10% coefficient of variation* value is derived by taking into account imprecision. It is the lowest value at which there are no analytic false positives due to imprecision. Many advocate use of this value.

5. Is imprecision the only problem with the assays?

No. There can be interfering substances, antibodies that cross-react with or bind to proteins used in the assay. Fibrin is the most common and can lead to false positives if samples are not adequately centrifuged. These problems should be rare but should be suspected whenever serial values stay constant and do not fit the clinical situation. Clinical laboratories should be able to troubleshoot all these issues if alerted to a problem.

6. Do all elevations of troponin have similar clinical importance?

No. They all imply cardiac injury, but the specific etiology will determine the clinical significance of a given elevation and guide appropriate clinical management. Reasons for elevations other than overt coronary artery disease are shown in the table. Some entities are quite common, for example, pulmonary embolism and congestive heart failure.

7. How does renal failure affect troponin values?

In patients with renal failure who present with acute coronary syndromes, elevation of either cTnI or cTnT has the same prognostic importance as it does in patients without renal failure. However, many dialysis patients have elevations of cTnT without a detectable acute coronary syndrome. This observation probably relates to the way in which the fragments are degraded; levels of cTnT are much more frequently elevated in patients with renal failure. Nonetheless, multiple studies have confirmed that such elevations identify patients at high risk for subsequent cardiac events, especially if concomitant left ventricular hypertrophy is present. For that reason, cTnT evaluation has now been approved by the US Food and Drug Administration for risk stratification of patients on dialysis.

8. Do all patients with troponin elevations need to be admitted to a hospital?

The clinician must be sure that the patient with troponin elevations does not have an acute illness that may progress. If an acute coronary syndrome or pulmonary embolism can be ruled out, the clinical assay being used is consistent, additional evaluation may be considered on an outpatient basis.

Not all patients who are admitted to the hospital need to be admitted to a specialized cardiac service. If an underlying disease (eg, hypotension due to an arrhythmia, gastrointestinal tract bleeding, sepsis) is exacerbating underlying coronary disease or directly causing cardiac damage, treating that primary disease process should be the primary objective. In my view, however, urgent cardiac consultation should be obtained to define the cardiac situation.

9. Is there still a role for CK-MB?

Not much. Measuring CK-MB may be of value when the initial cTnI or cTnT is elevated and there is a need to determine timing of the event, ie, acute or subacute. This same logic has been used for reinfarction, but in general those patients usually have easily discernible elevations of either cTnI or cTnT.

10. What do I do if I have questions or a difficult case?

The *Cardiovascular Update* Web site has additional material and references. Mayo Clinic Division of Cardiovascular Diseases or Mayo Medical Laboratories (800-533-1710) can provide information from individuals with expertise in this area.

February is Heart Month

Upcoming Courses

CONTINUING MEDICAL EDUCATION, MAYO CLINIC

To request additional information about a course or to register, unless noted otherwise, please call 800-323-2688, e-mail cme@mayo.edu, or visit www.mayo.edu/cme.

18th Annual State of the Art Echocardiography
Feb 20-24, 2005, Phoenix, Ariz
Cosponsored by the American Society of Echocardiography

Practice of Internal Medicine
May 2-6, 2005, Rochester, Minn

Controversies in Cardiovascular Disease
May 13-14, 2005, Rochester, Minn

10th Annual Mountain Course: Success With Failure: New Strategies for Evaluation and Treatment of Congestive Heart Failure
Aug 7-9, 2005, Whistler, BC

Mayo Clinic Cardiovascular Board Reviews
Sept 24-29, 2005, Rochester, Minn

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.

24th Annual Cardiovascular Conference at Snowshoe
Jan 31-Feb 2, 2005, Snowshoe, WVa
Directed by: H.M. Connolly, MD, FACC

Cardiology at Cancun
Feb 14-18, 2005, Cancun, Mexico
Directed by: A.J. Tajik, MD, FACC; G.S. Reeder, MD, FACC

27th Annual Cardiology at Big Sky
Feb 21-25, 2005, Big Sky, Mont
Directed by: D.R. Holmes, Jr, MD, FACC; R.A. Nishimura, MD, FACC; D.L. Packer, MD, FACC; C. Warnes, MD, FACC

ACC 2005
Mar 6-9, 2005, Orlando, Fla

OTHER EDUCATION OPPORTUNITIES

To request additional information about a course or to register, unless noted otherwise, please call 800-323-2688, e-mail cme@mayo.edu, or visit www.mayo.edu/cme.

Selected Topics in Internal Medicine
Feb 7-11, 2005, Lahaina, Maui, Hawaii

Frequently Encountered Clinical Ethical Dilemmas (II)
Feb 9-11, 2005, Rochester, Minn

A Multidisciplinary Update in Pulmonary and Critical Care Medicine
Apr 7-10, 2005, Scottsdale, Ariz
Phone: 480-301-4580; e-mail: mcs.cme@mayo.edu

At the recent American Heart Association meeting, Bernard J. Gersh, MD, received the AHA's Distinguished Achievement Award. Raymond J. Gibbons, MD, was chair of the Committee on Scientific Sessions Program.

Cardiology Recipients of Named Professorships: Standing, left to right, Thom W. Rooke, MD, John and Posy Krehbiel professor in vascular medicine; David R. Holmes, Jr, MD, Edward W. and Betty Knight Scripps professor in cardiovascular medicine in honor of George M. Gura, MD; Andre Terzic, MD, PhD, Marriott Family professor; Rick A. Nishimura, MD, Judd and Mary Morris Leighton professor in cardiovascular disease and hypertension in honor of Alexander Schirger, MD; A. Jamil Tajik, MD, Thomas J. Watson, Jr, professor in honor of Robert L. Frye, MD. Seated, left to right, Raymond J. Gibbons, MD, Arthur M. and Gladys D. Gray professor in honor of Howard A. Andersen, MD; Robert L. Frye, MD, Rose M. and Morris Eisenberg professor; James B. Seward, MD, John M. Nassef, Sr, professor in cardiology in honor of Burton M. Onofrio, MD.

Frank Cetta, Jr, MD (*right*), has been appointed chair of the Division of Pediatric Cardiology. He succeeds David J. Driscoll, MD, who has served in this role for more than 19 years.

Mayo Clinic
CARDIOVASCULAR UPDATE

Medical Editor: Margaret A. Lloyd, MD
Surgical Editor: Christopher G. A. McGregor, MD
Editorial Board: David L. Hayes, MD, Hartzell V. Schaff, MD, Rick A. Nishimura, MD, Lee A. Aase, Amy Knutson, Jane A. Jacobs, Marjorie G. Durhman
Managing Editor: Jane C. Wiggs, MLA, ELS
Art Director: Marjorie G. Durhman
Media Support Services Contributing Artists: Mary Ayshford, Peggy Chihak, Rick Madsen, Christine Nerland, Randy Ziegler, Stephen Graepel, T. Godlove
Web Site Editorial and Coding: Jane A. Jacobs, Melinda Klein

MAYO CLINIC

200 First Street SW
Rochester, Minnesota 55905
www.mayoclinic.org