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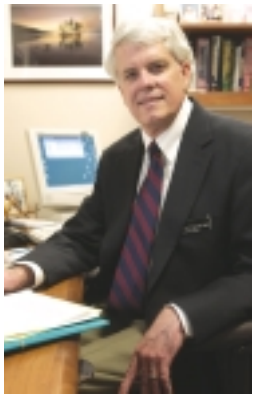
Syncope, Palpitations, Family History Should Cause Closer Look in Athletes' Physicals



Stephen C. Hammill, MD

When San Francisco State University basketball forward Richard Saunders collapsed and died suddenly during basketball practice, teammates and the public were stunned. Saunders was an apparently healthy 23-year-old, 6 feet 5 inches tall, who had played competitive athletics most of his life. This type of story causes great concern to the public and, of course, to the parents of young athletes. Of equal concern is the ability of the medical community to identify such patients early to prevent sudden death.

In high school, the athlete is a minor, the activity is extracurricular, and the athlete is considered an amateur. As athletes age through college, they gain independence as adults, their sport becomes a vocation, and there is significant personal and institutional financial incentive to pursue a career in athletics. "Identification and subsequent intervention should be aimed at younger athletes when it is easier to alter their lifestyle and redirect them to a sport or activity with less risk of sudden death," says Stephen C. Hammill, MD, director of Heart Rhythm Services at Mayo Clinic in Rochester.

Typically, athletes have a slower minimum heart rate, higher percentage of sinus pauses longer than 2 seconds, and more first-degree atrioventricular block, Mobitz I block, and junctional rhythm compared with controls. "The alteration in heart rate is caused by increased vagal tone in response to conditioning. This slower heart rate causes a compensatory increase in stroke volume to maintain cardiac output. Therefore, it is common for athletes to have increased left ventricular size but uncommon for them to have increased left ventricular wall thickness," says Dr Hammill.

In a report of 947 elite athletes participating in 27 sports, 38% had greater-than-normal left ventricular size, and only 2% had greater-than-normal left ventricular wall thickness. Sports accounting for the largest left ventricular size include rowing, cycling, and cross-country skiing.

The causes of sudden death in competitive athletes depend on their age. Among athletes less than 35 years old, approximately 50% who die suddenly are found at autopsy to have hypertrophic cardiomyopathy; 7%, a ruptured aorta; 10%, coronary heart disease; 18%, idiopathic left ventricular hypertrophy; and 14%, coronary artery anomalies. An additional 3% have an unexplained etiology; presumably these individuals have some type of an electrical abnormality such as long QT syndrome, Brugada syndrome, or idiopathic ventricular fibrillation.

By contrast, among athletes aged 35 years or older, 80% are found at autopsy to have severe coronary heart disease; 5%, hypertrophic cardiomyopathy; 5%, mitral valve prolapse; 5%, acquired valvular heart disease; and 5%, no identified cause.

A unique cause of sudden death in athletes is commotio cordis in which blunt chest impact from a projectile such as a baseball or a hockey puck results in sudden death. Ventricular fibrillation starts when the chest blow occurs during a critical window of repolarization (15-30 ms before the peak of the T wave).

Inside This Issue

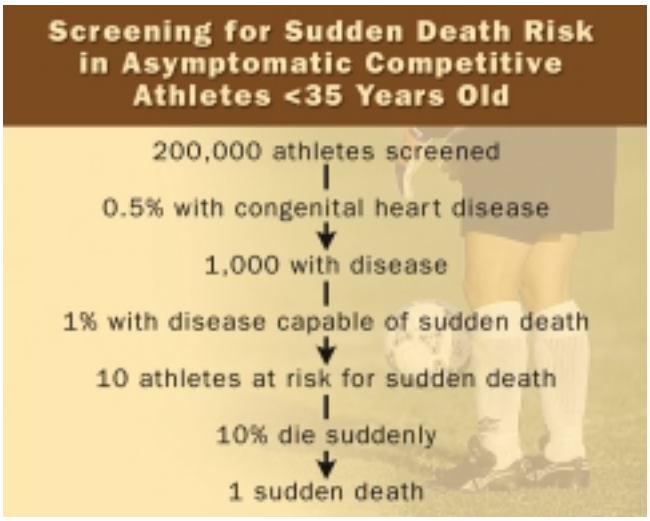


Figure 1. Screening asymptomatic competitive athletes younger than 35 years for risk of sudden death. (Data derived from Epstein and Maron. J Am Coll Cardiol. 1986;7:220-230.)

Screening for heart disease is difficult because of the large number of individuals who need to be screened to prevent just 1 sudden death. Epstein and associates reported on screening to prevent sudden death in asymptomatic athletes less than 35 years old (Figure 1). They estimated that 200,000 athletes would need to be screened to identify 1 athlete in whom sudden death could be prevented. Obviously, routine screening of every athlete is not feasible since there are about 5 million high school athletes, 400,000 college athletes, and 3,000 professional athletes in the United States.

Screening is equally difficult in competitive athletes who are asymptomatic and aged 35 years or older (Figure 2). In this scenario, if 10,000 asymptomatic men were screened, the overall risk for sudden death would be 0.5% per year. "One sudden death could be prevented in athletes with an abnormal stress test, but 4 sudden deaths would have occurred in the group with no risk factors and a normal stress test," says Dr Hammill. "Obviously, screening in this population would not be cost-effective."

Maron and associates investigated the prevalence of sudden death in 651,695 high school athletes in Minnesota between 1985 and 1997 and found 3 sudden deaths due to anomalous coronary artery, aortic stenosis, and myocarditis. The 3-year risk in this group of high school athletes was 1 in 72,500.

Screening the entire population of athletes is a difficult logistical task and often fails to identify patients who subsequently develop sudden death. Furthermore, published studies have included almost exclusively male athletes; whether these findings apply to female athletes is unknown.

Guidelines for determining athletic eligibility, formulated at the 1994 Bethesda Conference, have been published by the American College of Cardiology and the North American Society of Pacing and Electrophysiology. They recommend that athletes be screened initially with a history and physical examination. If the history identifies an individual with previous near syncope, syncope, palpitations, or a family history of sudden cardiac death or if the physical identifies a serious heart murmur or other cardiac problem, the athlete should undergo electrocardiography, echocardiography, and stress testing. Depending on the results of these tests, electrophysiologic testing or long-term monitoring should be considered. The subsequent decision to participate in sports is guided by the published guidelines that usually indicate that the affected individual should not participate in competitive athletics or should change to a less competitive sport. Hypertrophic cardiomyopathy is the most common abnormality identified during preparticipation screening of athletes, and affected individuals are advised not to participate in competitive sports.

The athlete presenting with syncope or palpitations needs to undergo a thorough history and physical examination along with ECG, stress testing, and echocardiography. If no heart disease is identified, further evaluation may include tilt testing and an event recorder. If heart disease is identified, further evaluation may include electrophysiologic studies followed by tilt testing or an event recorder if no serious abnormality is identified. The implantable loop recorder is uniquely helpful in athletes to record the ECG without artifact during spells that occur infrequently.

In summary, identifying the athlete at risk for sudden death is difficult because of the low incidence of sudden death in the large population of athletes. The athlete with a family history of sudden death or who presents with syncope or palpitations requires further medical evaluation and diagnostic testing. "The Bethesda Conference report provides clear recommendations for the expected standard of care that should be followed to determine whether to allow individuals to compete in a variety of different sports with different levels of intensity. It is a helpful document for the athlete's physician," advises Dr Hammill. Additional information can be obtained at the *Cardiovascular Update* Web site, www.mayoclinic.org/cardionews-rst.

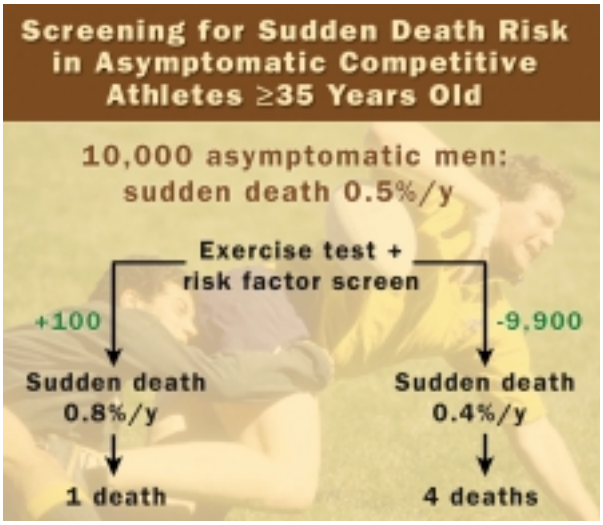


Figure 2. Screening asymptomatic competitive athletes aged 35 years or older for risk of sudden death. (Data derived from Epstein and Maron. J Am Coll Cardiol. 1986;7:220-230.)

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PET Scans Help Identify Patients With Potential Benefit From Revascularization

Panithaya Chareonthaitawee, MD

Positron emission tomography (PET) is a valuable diagnostic tool in the determination of myocardial viability and coronary flow reserve. The Mayo Clinic Positron Emission Tomography Imaging Center, operational since 2001, is closely aligned with the Division of Cardiovascular Diseases to provide optimal diagnostic testing. A team of Mayo Clinic cardiologists, nuclear medicine specialists, nurses, technologists, and other specialists perform studies on the two state-of-the art scanners (Figure 1). An on-site cyclotron has a dedicated staff to generate isotopes daily for clinical and research studies.

"Compared with conventional nuclear techniques, PET offers higher diagnostic accuracy as a result of its higher spatial and temporal resolution, as well as its built-in attenuation correction," according to Panithaya Chareonthaitawee, MD, Mayo Clinic nuclear cardiologist. PET tracers emit higher-energy gamma rays (511 keV) than conventional nuclear tracers (thallium-201, 70-80 keV, and technetium-99m sestamibi, 140 keV).

PET relies on the principles of positron emission. A positron is a positively charged electron emitted from the nucleus of a radioisotope that is unstable because it has an excessive number of protons. After traveling a short distance, the positron collides with an ordinary electron of a nearby atom in an annihilation reaction. This reaction turns the mass of the two particles into two 511-keV gamma rays or high-energy photons that are emitted opposite each other. These high-energy photons penetrate the human body easily and can be detected externally if a pair of detectors is set up along the coincidence line in a coincidence circuit (ie, coincidence detection). A radioactive "count" registers only when interactions are recorded simultaneously in the two detectors placed opposite one another. This helps accurate localization of counts.

"Current clinical application of PET imaging in cardiology can be divided into two main categories: detection of myocardial viability and assessment of coronary flow reserve," says Dr Chareonthaitawee.

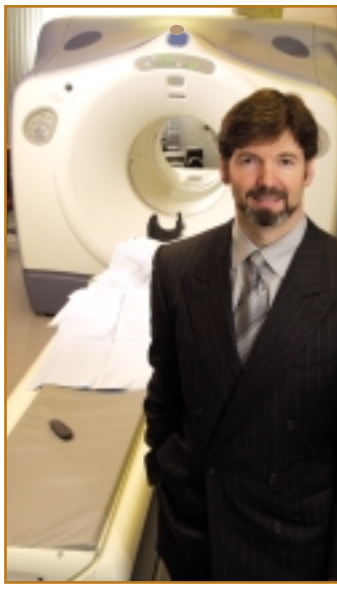
Detection of Myocardial Viability

In the United States, the growing number of patients with chronic ischemic left ventricular systolic dysfunction contributes to the increasing morbidity and mortality of heart failure. In patients with coronary artery disease, left ventricular systolic dysfunction is among the most important determinants of long-term prognosis. Survival rates decline in proportion to the severity of the left ventricular dysfunction. Coronary revascularization in specific subsets of patients with moderate to severe left ventricular dysfunction may lead to improved regional and global left ventricular function, improved quality of life, diminished heart failure symptoms, and improved long-term survival. Revascularization in such patients is also associated with higher risk, however. It is therefore critical to identify those patients likely to benefit most from revascularization procedures. Benefits appear to be greatest in a subset of patients with moderate or severe left ventricular dysfunction who have pronounced myocardial viability on noninvasive testing. In a recent meta-analysis, a 79.6% reduction in mortality occurred among patients with viability (identified by noninvasive testing) treated by revascularization. Patients without myocardial viability had no significant difference in mortality between revascularization and medical therapy.

Several techniques have been developed to identify dysfunctional but viable myocardium, including PET with F-18 fluorodeoxyglucose (FDG), single photon emission computed tomography (SPECT) with thallium-201 and technetium-99m sestamibi, and low-dose dobutamine echocardiography and MRI. Although the literature in this area has many limitations, PET offers the highest sensitivity and negative predictive accuracy for detection of improved resting regional contractile function after revascularization. "On the basis of the published literature and our prior experience with FDG PET studies, it is anticipated that about 15% of those patients with large fixed defects by technetium or thallium SPECT will have viability by PET," says Dr Chareonthaitawee. "Therefore, PET will potentially make a difference in one of every six such patients."

FDG, a glucose analogue, detects myocardial viability by tracing the initial transmembranous exchange of glucose from blood to tissue and its subsequent hexokinase-mediated phosphorylation. Unlike glucose-6-phosphate, phosphorylated FDG is not a substrate for the glycolytic pathway or for dephosphorylation and remains trapped within the myocyte.

Under normal conditions, the myocyte prefers to use free fatty acids for energy production; therefore,



PET imaging specialist Dr. Val J. Lowe with PET scanner.

myocardial glucose uptake and, proportionately, FDG uptake are relatively low. However, the ischemic myocyte preferentially uses glucose (anaerobically), leading to enhanced uptake of FDG, which is detected externally by the scanner. Viability studies are generally performed in conjunction with a resting perfusion scan. The traditional pattern of myocardial viability is the pattern of decreased flow and relatively enhanced metabolism (perfusion-metabolism mismatch) consistent with hibernating myocardium, which has a high likelihood of functional recovery after revascularization (Figure 2). Any region with relatively preserved FDG uptake (>50% normal) is also considered viable but the likelihood of recovery varies, depending of the degree of FDG uptake.

Although the amount of dysfunctional but viable myocardium required for improved global left ventricular dysfunction after revascularization is debatable, a recent study has suggested that a threshold of approximately one-third of the left ventricle provides the optimal cutoff between sensitivity and specificity.

Several guidelines can be used to identify suitable patients for PET myocardial viability studies:

- Left ventricular dysfunction (ejection fraction<40%)
- Evidence of coronary artery disease as the basis for the left ventricular dysfunction (previous myocardial infarction, coronary anatomy, other noninvasive imaging)
- Potential candidacy for revascularization by either percutaneous intervention or bypass surgery

A PET viability study may also be performed before coronary angiography. If viability is present, the patient may then proceed to coronary angiography. If viability is minimal, a less invasive approach may be considered. A PET study may also be performed in patients undergoing evaluation for potential cardiac transplantation. If viability is present, it is reasonable to reassess the likelihood of successful revascularization. In specific instances, the PET viability study may also be performed in patients with left ventricular ejection fraction of greater than 40% to determine viability in specific areas of prior infarction prior to percutaneous intervention. For patients who underwent previous SPECT imaging, PET may help define areas of moderately decreased tracer uptake and also may show viability in 15% of patients with large fixed severe defects by conventional imaging.

The Centers for Medicare and Medicaid Services (the renamed Health Care Financing Administration) recently approved coverage of FDG studies for assessment of myocardial viability as the primary or initial diagnostic study preceding revascularization and also covers FDG studies when they are used as follow-up to inconclusive SPECT.

Assessment of Coronary Flow Reserve

PET may also be used for the diagnosis of coronary artery disease and for the assessment of coronary flow reserve. The most commonly used PET perfusion tracers are N-13 ammonia, rubidium-82, and O-15 water. N-13 ammonia is rapidly extracted from the blood and is trapped in the myocardium by the glutamine synthesis reaction. Rubidium is an analogue of potassium, with biological behavior similar to that of thallium-201. Unlike the other two perfusion tracers, oxygen-labeled water is freely diffusible in the myocardium without dependence on metabolism.

The major advantage of rubidium-82 is that it is generator produced, and PET perfusion imaging can therefore be performed simply and economically without a cyclotron. Both N-13 ammonia and O-15 water are cyclotron produced. Rubidium-82 and N-13 ammonia images (Figure 3) are easier to interpret than O-15 water images.

Three reports have demonstrated the advantages of PET perfusion

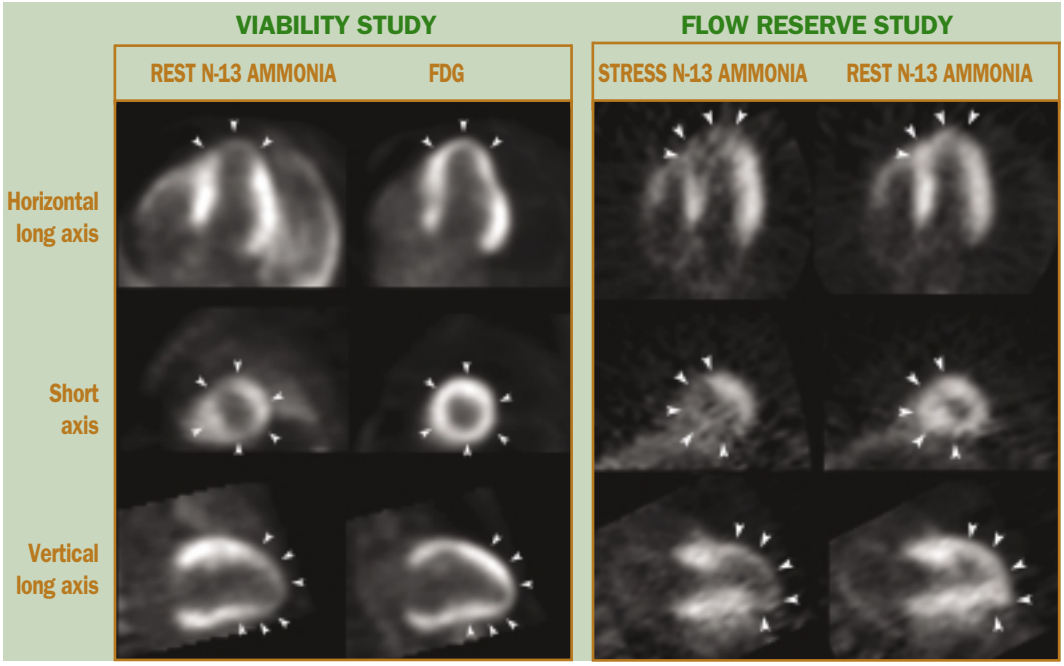


Figure 2. Example of PET perfusion-metabolism mismatch (decreased perfusion with relatively enhanced metabolism) in the apex, anterior, and anteroseptal regions consistent with hibernating myocardium in a patient with known ischemic cardiomyopathy. These regions recovered function after revascularization. The remainder of the left ventricular myocardium is also viable by PET.

Figure 3. Example of PET stress-rest perfusion (N-13 ammonia) study demonstrating a medium- to large-sized reversible apical and anterior defect consistent with ischemia.

imaging over conventional SPECT imaging. The first study showed similar high diagnostic accuracy for detecting coronary artery disease by either PET or SPECT but superior image quality and improved delineation of stress-induced ischemia with PET than with thallium-201 SPECT. The other two reports, which included larger numbers of patients suspected of having coronary artery disease, showed higher sensitivity and specificity with PET than with thallium-201 SPECT. In addition, the localization of perfusion defects was more accurately performed with PET than with SPECT. The overall accuracy of PET in the detection of obstructive coronary artery disease has been summarized as approximately 90% to 95% sensitivity and 85% to 90% specificity.

The Centers for Medicare and Medicaid Services recently also approved coverage of N-13 ammonia studies for the assessment of myocardial perfusion. Rubidium-82 has been covered for this indication for several years.

"Similar to other forms of cardiac stress testing, PET may be performed for the diagnosis of obstructive coronary artery disease, risk assessment, and prognosis and to guide therapy," says Dr Chareonthaitawee. PET may be particularly helpful in selected patients: those with large breasts and excess adipose tissue that may produce attenuation artifacts by conventional nuclear imaging but not by PET because of its built-in attenuation correction; patients with inconclusive SPECT images, including small mild or nonspecific defects by SPECT imaging; and patients with normal SPECT imaging with an appropriate chest pain syndrome consistent with angina.

A New Class of Patients: Adults With Congenital Heart Disease Need Lifelong Follow-up

Carole A. Warnes, MD
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Almost 1 million adults in the United States have congenital heart disease (CHD). Sometimes CHD is identified for the first time in adulthood; in many more cases, however, patients survive to adulthood because of cardiac surgery earlier in life. "Although operations for CHD have been performed at Mayo Clinic since the 1950s, there is no real cure for patients with CHD, and lifelong follow-up is necessary," according to Carole A. Warnes, MD, director of the Adult Congenital Heart Disease Clinic at Mayo Clinic.

Patients are vulnerable to arrhythmias, ventricular systolic and diastolic dysfunction, development of pulmonary hypertension, and progression of valvular problems. Pregnancy is possible for the majority of women with CHD, but prepregnancy counseling and careful selection are mandatory as is combined cardiac and obstetric care antepartum, during pregnancy, and peripartum. Patients with CHD also need advice about general medical issues such as exercise guidelines and employment. They may also be at special risk during noncardiac surgery, particularly if they have cyanotic CHD. Frequently patients are not well educated about their CHD and know surprisingly little about what their future might hold, says Dr Warnes.

The Adult Congenital Heart Disease Clinic brings together a multidisciplinary team of physicians with special training in adult CHD. The clinic, created 15 years ago to address the special needs of this growing population, now follows almost 3,000 patients. Most patients seen in the clinic are between 20 and 30 years old, but almost 40% of patients are older than 40 years because good medical and surgical care has extended their lives (Figure 1). Adult CHD patients are also vulnerable to acquired medical and cardiovascular problems such as hypertension, diabetes mellitus, and coronary artery disease.

In the Adult Congenital Heart Disease Clinic, a comprehensive approach is taken for evaluation of patients' disorders, including thorough education of patients and their families about the cardiac anatomy and important medical issues such as endocarditis prophylaxis. A history and clinical evaluation are performed. Exercise testing is particularly helpful in these patients, who, having lived with a congenital anomaly, may believe their functional capacity is normal, when in fact it may be more limited. Specialists in CHD perform detailed tests such as echocardiography, which, in many cases, obviate the need for cardiac catheterization. Transesophageal echocardiography or magnetic resonance imaging may be required in complex cases when additional information is needed after transthoracic imaging. When necessary, care is integrated with other specialists such as high-risk obstetricians and specialists in pulmonary hypertension.

At Mayo Clinic in Rochester, primary and repeat operations in patients with congenital heart defects are performed by cardiovascular surgeons with additional training and expertise in CHD. "In general, cardiac reoperations are associated with higher operative mortality than first operations," says Joseph A. Dearani, MD, Mayo Clinic cardiac surgeon. Studies have demonstrated that operative mortality is reduced when experienced surgeons in high-volume centers perform operations for CHD. "The operative mortality for adults with CHD at Mayo Clinic in

the last 15 years is 3.5%, even though more than 30% of patients have undergone at least 3 operations," says Dr Dearani (Figure 2).

Patients with adult CHD have complex management issues that differ from those found in a routine cardiology practice. Diagnosis and detection of associated lesions, management of arrhythmias, and timing of operation require comprehensive knowledge of the heart's anatomy and pathophysiology and the natural history of CHD. Specific problems involving the right ventricle and pulmonary vascular disease often result in late referral, which is frequently beyond the optimal time for surgical intervention.

Common cardiac anomalies seen in patients in the Adult Congenital Heart Disease Clinic include tetralogy of Fallot and coarctation of the aorta. In tetralogy of Fallot, the most common late problem is related to the right ventricular outflow tract and pulmonary valve. Long-standing pulmonary valve regurgitation may result in the development of late problems, including right ventricular dilation with progressive tricuspid regurgitation, heart failure, atrial and ventricular arrhythmias, and even sudden death. Close cardiovascular monitoring for arrhythmias and progressive right heart enlargement is indicated after repair of tetralogy of Fallot, and pulmonary valve replacement is often required in this patient group. According to Dr Warnes, lack of adequate medical follow-up and late referral are major causes of morbidity and mortality in patients with tetralogy of Fallot.

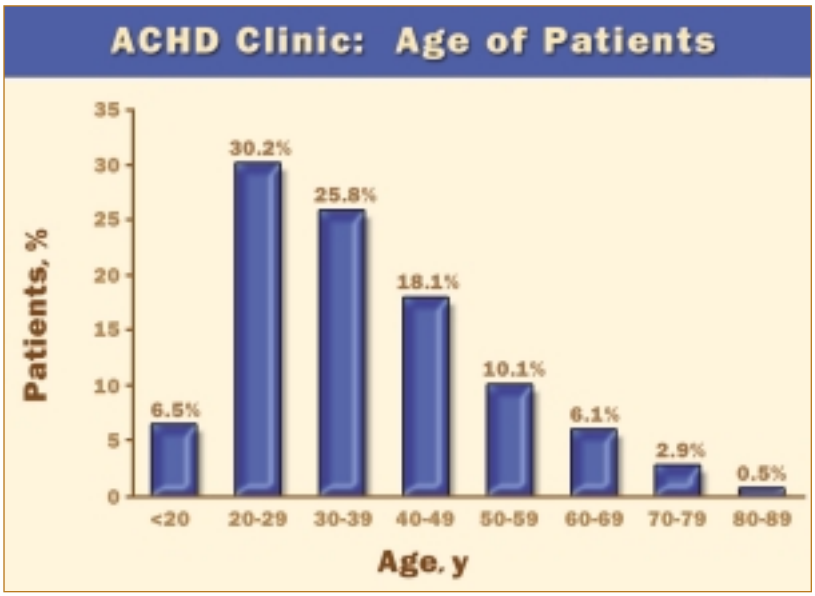

Figure 1. Age distribution of patients seen in the Adult Congenital Heart Disease Clinic.

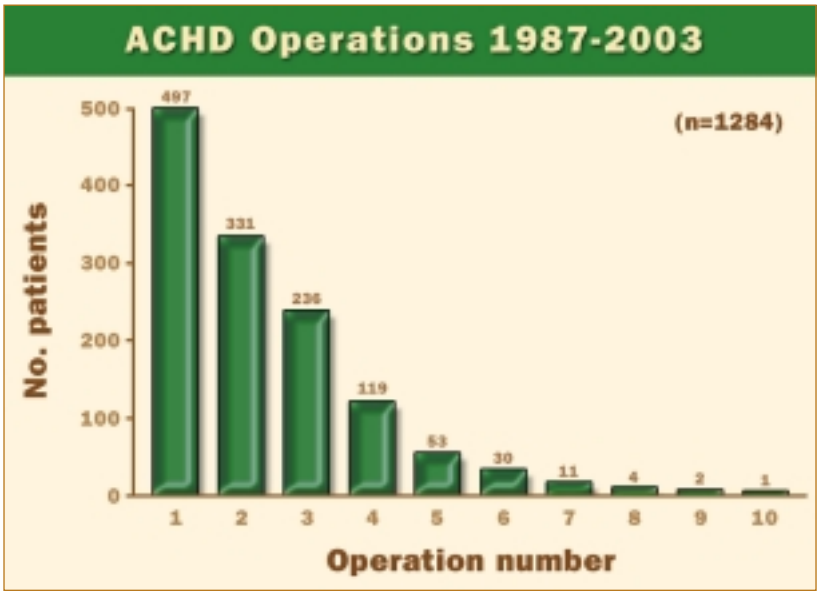

Figure 2. The number of congenital cardiac operations performed through the Adult Congenital Heart Disease Clinic between 1987 and 2003. Over one third of patients have had 3 or more operations. The operative mortality for all cases was 3.5%.

Surgical repair of coarctation of the aorta has been performed since the 1940s. Life expectancy is markedly improved after surgery but is not normal. Some concerns that continue after surgery include persistent hypertension and an increased risk of cardiovascular complications, including myocardial infarction, congestive heart failure, stroke, recoarctation, and other aortic problems. "Patients with coarctation are also more likely to have a bicuspid aortic valve, which may become stenotic or regurgitant," says Dr Dearani. In addition, patients with a history of coarctation are also at increased risk for development of intracranial aneurysms. Careful follow-up by a cardiologist aware of the complications that can arise after surgical repair of coarctation is essential for improved patient outcome.

Comprehensive review of specific congenital cardiac abnormalities and syndromes will appear in future issues of *Cardiovascular Update*.

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14th Annual Echo Hawaii 2004
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9th Annual Cardiology at Cancun 2004
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Cardiologist Raymond J. Gibbons, MD, is chair of the 2003 American Heart Association Committee on Scientific Sessions.

2003 pediatric cardiology training program, Mayo Clinic in Rochester. Back row, left to right, are staff pediatric cardiologists Donald J. Hagler, MD; Co-burn J. Porter, MD; David J. Driscoll, MD; Douglas D. Mair, MD; Allison K. Cabalka, MD, training program director; Timothy M. Olson, MD; and Patrick W. O'Leary, MD. Front row, left to right, are trainees Norbert H. Yoe, MD; Michael G. Earing, MD; Ritu Chatrath, MD, graduating and relocating to Arkansas Children's Hospital, Little Rock; and Anant Khositseth, MD, graduating and relocating to Bangkok, Thailand. Not pictured is pediatric cardiologist Michael J. Ackerman, MD, PhD.

Laser Relieves Angina in Patients Unsuitable for Bypass Surgery or Balloon Angioplasty

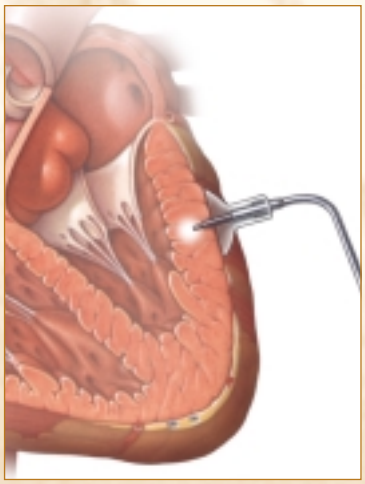
Charles J. Mullany, MD

For most patients with symptomatic coronary artery disease, treatment consists of medical therapy (nitrates, β-blockers, aspirin, and lipid-lowering agents) and, in many instances, revascularization by either percutaneous transluminal coronary angioplasty (PTCA) or coronary artery bypass graft (CABG) surgery. "Transmyocardial revascularization (TMR) offers an alternative form of treatment for severely symptomatic patients who are unsuitable for either primary or repeat revascularization," according to Charles J. Mullany, MD, a cardiovascular surgeon at Mayo Clinic in Rochester. In addition, TMR may be used as adjunctive therapy during either primary or repeat CABG surgery to treat those areas of the ischemic myocardium that cannot be revascularized directly, says Dr Mullany.

Numerous clinical studies, including at least 5 randomized clinical trials, have evaluated use of either the CO_2 laser or the holmium:YAG laser. As a consequence, TMR with laser has been approved by the US Food and Drug Administration for the treatment of patients with severe angina pectoris.

Candidates for stand-alone TMR include patients who have class III or IV angina and who are not candidates for either CABG or PTCA. Most patients (90%) will have had prior CABG, PTCA, or both. Approximately 50% of such patients also have diabetes mellitus. In previously published randomized trials, most patients who have undergone isolated TMR have a patent left internal mammary graft to the left anterior descending coronary artery with severe ischemia of other coronary territories.

Patients who do not have anginal symptoms and whose symptoms are principally those of heart failure are not candidates for TMR. Poor left ventricular function (ejection fraction<30%), recent myocardial infarction, and unstable symptoms are relative contraindications to the procedure.



Holmium:YAG laser probe on the external myocardial surface.

"Most of the mortality associated with TMR occurs in patients with unstable angina, poor left ventricular function, or both," says Dr Mullany. "In these patients, use of an intra-aortic balloon pump at the same time as TMR may be beneficial."

TMR, without concomitant CABG, is usually performed through a limited left anterolateral thoracotomy and does not require that sternotomy be repeated. After exposure of the myocardium, between 20 and 30 transmural channels are created with the laser device. Most patients tolerate the procedure well and can be discharged from the hospital within 4 days of surgery. Operative mortality is less than 2%. Patients continue to take their antianginal medications because myocardial ischemia persists despite the absence of angina.

Angina is relieved in up to 70% of well-selected patients. In 5 randomized clinical trials comparing laser with maximal medical therapy, clinical improvement in angina status occurred in 58% of patients undergoing TMR compared with 11% in control patients. In most instances, relief of angina occurs over several weeks to months after the procedure. A number of patients experience angina relief immediately after the procedure and before hospital discharge.

Clinical studies have consistently found relief of angina, improvement in quality of life, improved exercise tolerance, decreased need for antianginal medications, and reduced rate of readmission to the hospital for unstable angina in the year after TMR. Despite these subjective improvements, however, objective measures of improvement have not been consistent in these studies. Most investigators have not demonstrated improved regional myocardial blood flow with use of nuclear imaging. The results of exercise testing have also been mixed. In addition, most studies have not demonstrated an increase in ejection fraction after TMR. In the Atlantic study (TMR with holmium:YAG laser versus medical therapy), patients treated with TMR had an increase in heart failure symptoms in the 12 months after TMR. No improvement in survival has been demonstrated in patients undergoing TMR.

The mechanism whereby TMR relieves angina pectoris is unknown. Initially it was believed that channels created by the laser functioned like sinusoids to deliver blood from the ventricular lumen directly to the myocardium. In humans, most channels created by the laser do not maintain long-term patency, closing within 2 weeks of TMR. A placebo effect may be responsible for improving clinical symptoms.

The mechanism of action of TMR may be angiogenesis. The nonspecific thermal injury induced by laser therapy (CO_2 or holmium:YAG) may result in the local release of growth factors and subsequent angiogenesis. Theoretically, therefore, laser therapy may be enhanced by delivering angiogenic growth factors (vascular endothelial growth factor, fibroblast growth factor, and platelet-derived growth factor) directly to the ischemic tissue at the same time as the laser therapy.

In conclusion, TMR is appropriate treatment for patients who have intractable class III or IV angina and who are not candidates for CABG or PTCA. Preferred candidates are those with stable symptoms and reasonably well-preserved left ventricular function (ejection fraction>30%). In well-selected patients, angina is relieved, and quality of life improves. "Operative mortality in such patients should be less than 2%, although there is no improvement in long-term survival," says Dr Mullany.