



# The Johns Hopkins Heart Institute Cardiovascular REPORT

**FOCUS ON HYPERTROPHIC CARDIOMYOPATHY**

**SPRING 2007**



Ted Abraham and John Resar

## Ousting the 'O' in HOCM

**When obstructed left ventricular outflow becomes disabling, the right treatment can restore quality of life.**

**THE CASE:** Until two years ago, when she began noticing how easily she became winded, the 76-year-old had little reason to suspect that her heart was anything but healthy. She'd been told at 18 that she had a murmur but had been assured that it was benign and insignificant. She didn't smoke or drink, had no history of hypertension and had never had a heart attack. Still, there were two instances when she passed out while running on a treadmill, and over the preceding six months her shortness of breath had worsened to the point that she could barely walk 15 yards.

The patient's internist referred her to a cardiologist, who immediately ordered an echocardiogram. Concerned because the imaging showed walls that looked slightly thick, the specialist turned to Hopkins' **Theodore Abraham** with two questions: Does this patient have hypertrophic cardiomyopathy? If so, can you help me manage her care?

**THE HOPKINS APPROACH:** Abraham, director of the Johns Hopkins Hypertrophic Cardiomyopathy Clinic, and his colleagues have created a systematic clinical program aimed at teasing out what is not always an obvious diagnosis. Their first step is a detailed panel consisting of conventional echocardiography, treadmill stress echo, tissue Doppler strain echo and contrast echo.

In this patient's case, results showed a wall thickness of 1.8 to 2.0 cm, no apical hypertrophy, no significant wall motion and mild resting left ventricular outflow tract (LVOT). Her resting gradient, 26 mm/Hg, increased to 40 mm/Hg with the Valsalva maneuver and to 75 mm/Hg with amyl nitrite administration.

When the patient exercised on a modified Bruce protocol, the test was stopped at five minutes because of her fatigue and dyspnea. An EKG showed baseline T-wave inversions that did not change with exercise. Her base-

line wall motion became hyperkinetic with exercise, and her peak exercise LVOT gradient increased to 120 mm/Hg. On tissue Doppler, her regional strain was 4 percent in the anterior septum despite normal wall motion and ejection fraction.

Despite the absence of the classic echocardiographic features, the patient's low regional strain and high outflow gradients by exercise, Abraham's diagnosis was hypertrophic obstructive cardiomyopathy with a significant outflow gradient. Although the patient had initially given no history suggesting familial HCM, when Abraham referred her to cardiac geneticist **Daniel Judge** for evaluation, she remembered that both her mother and a maternal uncle had had murmurs. During subsequent family screening, Judge found that her brother's daughter also has HCM.

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# Consultation: Sunil Sinha

Director, Arrhythmia Device Clinic, Johns Hopkins Heart Institute

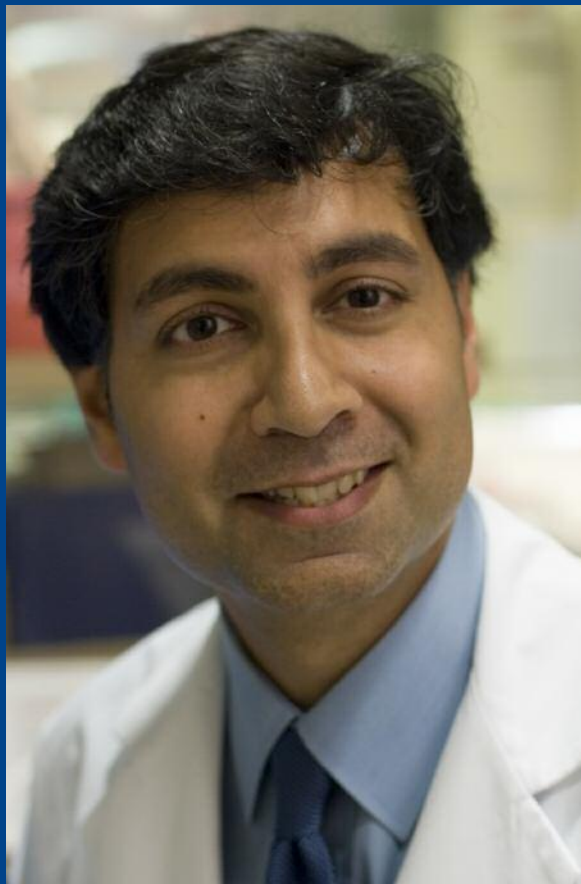
## What puts patients with hypertrophic cardiomyopathy at risk of sudden cardiac death?

The primary culprits are ventricular tachycardia and ventricular fibrillation. Bradyarrhythmias are also on the list. Severe obstructive cardiogenic shock may occur in advanced cases.

We believe VT/VF is facilitated by the underlying substrate of disordered LV myocardial architecture that can trigger and maintain the arrhythmias. Some patients probably experience episodic myocardial ischemia, which results in necrosis and fibrosis and adds to the problem. Hypoxemia and catecholamine release during severe exertion can further increase risk.

## Are there ways to stratify sudden cardiac death risk in HCM patients?

Yes, though it's an inexact science. The most ominous sign, of course, is cardiac arrest or spontaneous sustained VT. But among patients who haven't had a serious event, several major risk factors have been identified, including nonsustained ventricular tachycardia on ambulatory monitoring, a family history of SCD in close relatives, otherwise unexplained syncope, left ventricular wall thickness that measures 30 mm or more, and abnormal blood pressure response—blunting or a decrease—during a routine treadmill stress test. LV outflow obstruction, an identified



high-risk mutation or intense physical exertion represent significant risk factors in certain patients.

## What's the best way to minimize the risk of SCD in these otherwise healthy patients?

Patients who've had aborted sudden cardiac death or cardiac resuscitation are known to benefit from an implantable cardioverter defibrillator for secondary prevention. In those at high risk and already receiving optimal medical therapy, an ICD is indicated for primary prevention. We recommend routine follow-up every three months post-insertion. With newer devices equipped with a radiofrequency antenna, we can perform remote ICD analysis and download interrogation data from a secure Web site, reducing the frequency of in-clinic checks.

## Can athletes with an ICD still participate in their sport?

HCM is believed to be the most common cause of sudden death in young competitive athletes. Many are extremely motivated, and it's tough for them to accept that even with an ICD, they're not immune to sudden death, as device malfunction or "refractory VT/VF" may uncommonly occur. So I'll only clear them for moderate aerobic activities and workouts in an accompanied setting, but not to play collegiate sports.

## Ousting the O

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**TREATMENT DECISION:** Abraham explained to the patient that her murmur was probably due not to an intrinsic valve problem but to her high LVOT gradient and that the options for relieving the obstruction included medical therapy, surgical septal myectomy or alcohol septal ablation. The patient and Abraham initially chose a six-month beta blocker trial (starting dose of 50 mg per day increased to 200 mg per day over four weeks). During this time, she returned to her referring cardiologist for Holter monitoring, which showed frequent, nonsustained ventricular tachycardia. Furthermore, because she developed significant fatigue, and a repeat echocardiogram showed that her provoked LVOT gradient remained high at 70 to 90 mm/Hg, her cardiologist asked her to return to Hopkins to discuss other interventions.

On her return visit to Hopkins, Abraham reviewed the two primary interventional op-

tions—surgical myectomy and alcohol septal ablation—with the patient, her family and her referring cardiologist. Given her age, lack of concomitant valve abnormalities, focal myocardial hypertrophy and personal preference, the consensus was to proceed with alcohol septal ablation, and the patient was referred to interventional cardiologist **Jon Resar**. Since her Holter monitor had showed nonsustained VT, she was also referred to arrhythmia specialist **Sunil Sinha** for further arrhythmia risk stratification and consideration for an implantable defibrillator.

Meeting with Sinha, the patient learned that several factors, including her nonsustained VT on Holter monitoring and her history of syncope, put her at increased risk for sudden cardiac death.

**THE PROCEDURE:** Resar performed the ablation, working with cardiac imaging specialist **Katherine Wu**. They visualized the patient's coronary anatomy via angiography to identify the possible arteries supplying the

basal septum, then injected an echocardiographic contrast agent through a balloon catheter to home in via echo on the area to be ablated. After slowly injecting alcohol 2 cc through the balloon catheter, Resar measured the patient's LVOT gradient. As it does in most cases, the gradient dropped immediately (from 40 mm/Hg to 5 mm/Hg), but had it not decreased, Resar would have repeated the alcohol injection in another septal artery.

**OUTCOME:** Following the procedure, Resar transferred the patient to the coronary care unit, where she was monitored for the next 24 hours with a temporary pacing catheter in case she developed sudden, complete heart block. She was discharged to the care of her referring cardiologist on a beta blocker and returned two weeks later for implantation of a cardioverter defibrillator because of her VT. Four weeks later, under the care of her referring cardiologist, she reported having approximately double her previous exercise capacity. ■

## Genetic Knowledge Means Treatment Power

To busy clinicians, the news that gene X has been linked to disease Y can seem about as relevant to patient care as the discovery of mountains on one of Saturn's moons. Yet in the case of mutations known to drive inherited hypertrophic cardiomyopathy, what was once solely the domain of researchers has morphed into a valuable diagnostic tool.

"It's too soon to say that all the genes have been identified," says cardiac geneticist **Daniel Judge**, "but we now have clinical tests that can identify a genetic cause for up to 70 percent of people with HCM."

In families where the sudden death of one member is the first inkling of HCM, for example, the test can determine who else carries culprit mutations. "HCM is usually easy to diagnose," says Judge, "but when there's borderline or normal wall thickness, it can be more challenging. If a genetic mutation is found in a clearly affected family member, this test can be



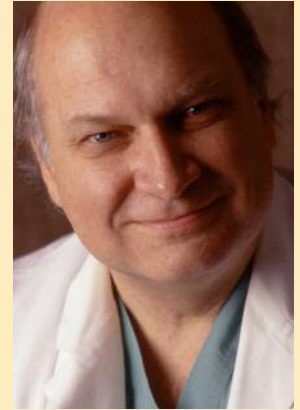
**Dan Judge and Nicole Johnson believe counseling is key.**

used within the family to identify presymptomatic patients."

Judge advises genetic counseling for all patients and families with inherited heart disease. Because the inheritance pattern is usually autosomal dominant, relatives often face a 50 percent chance of carrying the defective gene. "I won't order the genetic test without counseling," he says. Among the myriad issues that certified genetic counselor Nicole Johnson helps at-risk family members grapple with are understanding their likelihood of inheriting this condition and determining their best screening options. ■

## MYECTOMY: OLD BUT STILL GOLD

In the four decades since former Hopkins trainee Andrew Morrow pioneered myectomy, the procedure has proven to immediately—and permanently—alleviate severe, drug-refractory left ventricular outflow obstruction that can undermine quality of life in patients with hypertrophic cardiomyopathy.



**Duke Cameron**

And thanks to technical advances over the past 15 years, the operation is remarkably safe: When it's performed by an experienced surgeon in patients, including children, who meet established criteria, mortality rates often approach zero.

Still, observes cardiac surgeon **Duke Cameron**, the procedure isn't free of challenges. "It's not so much shaving a mound of tissue as it is cutting a trough to create another way for blood to leave the heart," he says. "You can't cut out all the muscle, but you do have to cut enough." Techniques such as intraoperative echocardiography help keep tabs on that progress, yet it's still critical to avoid nicking into the nearby aortic and mitral valves and the heart's electrical conduction system.

In short, says Cameron, "myectomy requires a surgeon who's trained and comfortable doing it. It also requires a whole team of collaborative specialists to decide what's best for the patient."

## THE RAREST INTERVENTION

One of the least likely outcomes associated with hypertrophic cardiomyopathy is eventual progression to heart failure. Sometimes unceremoniously referred to as "burn-out," it occurs in only about 5 percent of HCM patients. There is some evidence suggesting that individual HCM genetic mutations may underlie the condition; environmental factors also have been postulated as a cause. Whatever its origins, end-stage HCM is typically characterized by left ventricular wall thinning, dilation of the cardiac chambers (especially the left ventricle) and systolic dysfunction.

"Patients go from having a normal ejection fraction to one that's significantly reduced," says **Stuart Russell**, clinical director of Hopkins' Heart Failure and Cardiac Transplantation Service. "If that happens, we treat them as heart failure patients with a history of HCM."

Some can be managed with medical therapy; others require a ventricular assist device. Less than 1 percent will need a heart transplant. "We only consider transplantation when all else fails," says Russell, "and with all the other treatments we have, that's highly unlikely." ■

## Teaching Rounds

## The Art of Alcohol Ablation

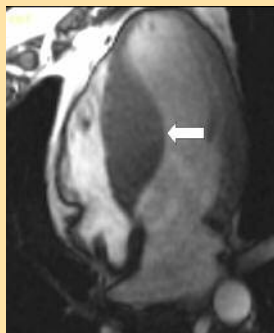
Take any basic definition of the two methods for relieving severe obstruction in hypertrophic cardiomyopathy and both sound straightforward. In myectomy, the surgeon resects a small area of the myocardial septum, forming a channel that expands the left ventricular outflow tract. In septal ablation, the interventional cardiologist infuses alcohol into one or more coronary artery branches that supply the septum, creating an infarction to reduce the outflow gradient. Yet ask anyone who performs these procedures, says interventionalist **Jon Resar**, and you'll find that each requires even more than advanced technical skill to achieve optimal patient outcomes.

In the case of alcohol ablation, there's a fine art to locating and injecting the correct vessel. Miss the branch of the left anterior descending coronary artery (LAD)

that's feeding the hump of septal muscle and there's likely to be residual obstruction—a result rare with myectomy.

Key to not destroying the wrong area of muscle, Resar says, is to properly identify the correct branch of the LAD that supplies the heart muscle via echocardiography and contrast agent before injecting the alcohol. The largest branch isn't always the one supplying the septal bulge, he points out. Instead, the culprit going to the left basal side of the septum may be an accessory branch.

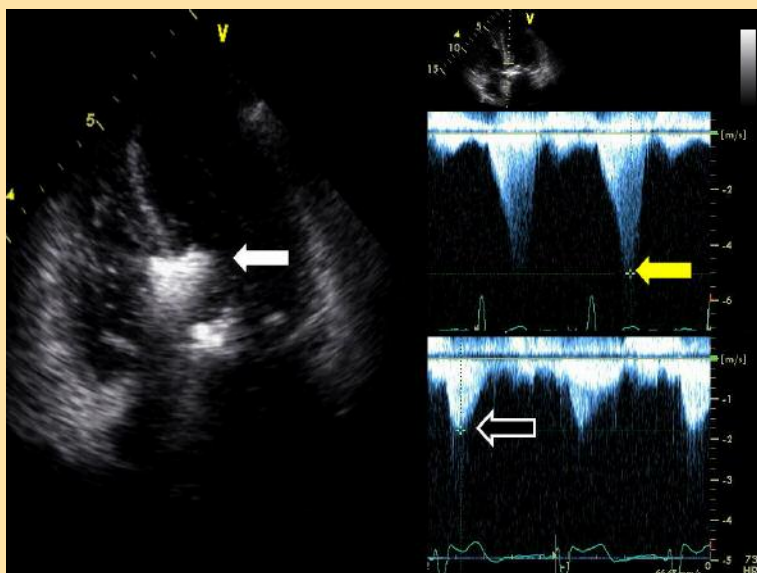
Because both myectomy and alcohol ablation entail risk of complete heart block, Resar adds, "we always consider each patient's risk factors for ventricular arrhythmia and sudden cardiac death. We know defibrillators have a huge effect on outcomes in this patient population." ■



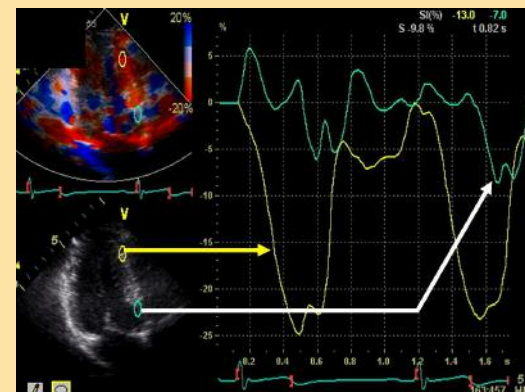
**Figure 1:** Magnetic resonance image illustrating a four-chamber view of the heart in a patient with significant septal hypertrophy (arrow).



**Figure 2:** An apical long view of the left ventricle by echocardiography with color flow Doppler illustrating turbulent flow in the left ventricular outflow tract due to systolic anterior motion of the mitral valve (white arrow) and eccentric, posteriorly directed mitral regurgitation (yellow arrow).



**Figure 3:** An apical long view of the left ventricle illustrating the presence of contrast in the hypertrophied basal septum (white arrow) during an alcohol septal ablation. Doppler interrogation of the left ventricular outflow tract demonstrated a significant reduction in outflow gradient from a pre-ablation level of 102 mmHg (yellow arrow) to a post-ablation level of 12 mmHg (black arrow)



**Fig 4:** Echocardiographic strain imaging of the left ventricle in the apical long view. The hypertrophic basal segment (white arrow; green tracing) shows substantially reduced strain of 6 percent compared to the normal-appearing apex (yellow arrow and tracing), which demonstrates a strain of 25 percent.

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