Is septal ablation preferable to surgical myomectomy for obstructive hypertrophic cardiomyopathy?

Surgical Myectomy Remains the Primary Treatment Option for Severely Symptomatic Patients With Obstructive Hypertrophic Cardiomyopathy

Barry J. Maron, MD

The evolving alcohol septal ablation versus surgical myectomy controversy represents a crossroad in the management of obstructive hypertrophic cardiomyopathy (HCM). Indeed, in this now polarized debate within the cardiovascular community, between the traditional and established (ie, surgery) and the new and percutaneous (ie, ablation), much is at stake for the HCM patient population. Furthermore, this issue has become increasingly important given the visibility recently afforded the pathophysiological significance and frequency of left ventricular (LV) outflow gradients in this disease.1,2

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In the course of this discussion, I will vigorously defend surgery as the primary treatment of choice when outflow obstruction (gradient ≥50 mm Hg at rest or with physiological exercise) produces heart failure symptoms refractory to maximal medical management (New York Heart Association functional classes III and IV).3,4 To this purpose, I will rely on the 50-year experience and substantial body of evidence available in HCM, as well as my own personal extensive association with and work in this disease spanning >30 years and several hundred publications—neither as a surgeon or interventional cardiologist nor with any particular allegiance to either discipline. The message expressed herein is prosurgery, but it is by no means antiablation, for this treatment modality has proved useful (although with a selective role) in the management of HCM.

Surgical Septal Myectomy

Historical Context

When surgical septal myectomy (Table 1) was initially introduced in the early 1960s at several North American and European centers, it was regarded as revolutionary and has subsequently stood the test of time. The classic myectomy (Morrow operation)5 relieves obstruction by resection of a relatively small amount of muscle (2 to 5g) from the proximal ventricular septum, thereby widening the outflow tract and abolishing flow drag (or Venturi) forces that promote systolic contact between mitral valve and hypertrophied septum, resulting in immediate gradient reduction6,7 (Figure 1). More recently, some surgeons have creatively modified the myectomy resection to be wider and to extend more distally, allowing more complete reconstruction of the LV outflow tract, which may be necessary in some patients.8–12
Dr. W.P. Cleland at Hammersmith Hospital (London) was the first surgeon to perform a myectomy, but the operation was soon abandoned in the United Kingdom for decades. Thereafter, Drs. Andrew Morrow at the National Institutes of Health, John Kirklin at the Mayo Clinic, and Wilfred Bigelow and William Williams at Toronto General pioneered surgical intervention (first myotomy and then myectomy), permitting surgical myectomy to emerge as the primary treatment option for severely symptomatic drug-refractory patients with outflow obstruction in many centers throughout the world.

Operative Risk

In its early years, myectomy was accompanied by ≥5% procedural mortality. Although such operative risk is now clearly obsolete, surgery continues to be frequently misrepresented as an outdated and risk-prone option by its opponents.

Over the last 15 years, with the advantage of contemporary cardiac preservation techniques and intraoperative echocardiography, myectomy has been associated with remarkably low operative mortality approaching zero at major centers (Figure 2). In the combined and continuing experience of the Mayo Clinic, the Cleveland Clinic, and Toronto General Hospital over the last 10 to 12 years, >1500 consecutive isolated myectomy operations have been performed without a postoperative death. The Mayo Clinic also reports no operative deaths in young children over this period (n=56). It is essential that this very low operative mortality risk, rather than irrelevant data transposed from the very early surgical experience, be cited to current myectomy candidates.

Heart Failure Benefit

The vast amount of data assembled worldwide over 40 years clearly substantiates that myectomy results in immediate and permanent abolition of mechanical obstruction to LV outflow (and mitral regurgitation) with normalization of LV pressures. As a consequence, surgery achieves relief and often elimination of disabling heart failure symptoms and restores exercise capacity and quality of life. In the most recent long-term postoperative analysis, almost 85% of patients became asymptomatic or only mildly symptomatic (New York Heart Association class I or II) an average of 8 years (and up to 25 years) after myectomy. No evidence exists that myectomy itself increases arrhythmogenicity or predisposes to systolic dysfunction and the end stage.

Furthermore, the preponderance of evidence from observational, comparative studies with alcohol septal ablation shows that myectomy affords more consistent and complete hemodynamic and symptomatic benefit and is associated with fewer procedural complications and reinterventions.

Survival Benefit

In addition to heart failure reversal, myectomy also promotes long-term survival. Operated patients experience enhanced longevity indistinguishable from that expected in the general population and superior to that of nonoperated patients with obstruction. After myectomy, survival free from all-cause mortality is 98%, 96%, and 83% at 1, 5, and 10 years, and survival free from HCM-related mortality (heart failure and sudden death) is 99%, 98%, and 95%, respectively. Therefore, surgical septal myectomy favorably alters the natural course of HCM, providing a reasonable expectation for normal or nearly normal life expectancy.
should not, however, be interpreted as a justification for intervention with either surgery or alcohol ablation at a much earlier time in the clinical course of HCM.

These substantial benefits of myectomy constitute compelling evidence supporting surgery as the gold standard treatment.3 In contrast is the unsettling and unsubstantiated claim by some in the interventional cardiology community that surgery should be marginalized or abandoned, has no significant role in the management of HCM, or in fact has already been usurped by alcohol ablation.33–35,41,42,52 Furthermore, given the available data, it seems somewhat less than respon-

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**Figure 1.** Septal myectomy operation. Classic surgical strategy as originally depicted by Dr Andrew G. Morrow. Rectangular myectomy trough (length, ~3 to 4 cm) from just below aortic valve to beyond site of mitral–septal contact and intraventricular obstruction. Some myectomy surgeons now routinely extend this resection more distally. From Maron et al97 with permission from the publisher. Copyright © 1983, Oxford University Press.

**Figure 2.** Contemporary low operative risk. Consecutive number of isolated septal myectomies (without associated cardiac operations or prior alcohol ablation) successfully performed since the last operative death at the 3 most active North American surgical centers: Mayo Clinic (Joseph Dearani, Gordon Danielson, Hartzell Schaff); Cleveland Clinic (Bruce Lytle, Nicholas Smedira); and Toronto General Hospital (William G. Williams, Anthony Ralph-Edwards). *Data to end of 2005. †Includes only adult patients. ‡Includes 2 relatively new myectomy programs: Roosevelt-St Luke’s Hospital Center (Daniel Swistel) and Tufts-New England Medical Center (Hassan Rastegar), each with no operative deaths (n=51 and n=38, respectively).

**Figure 3.** Survival benefit from surgical myectomy. Survival from all-cause mortality after isolated myectomy at the Mayo Clinic (gold) does not differ from matched general US population (white) \( P=0.2 \) and is superior to nonoperated HCM patients with obstruction (green) \( P<0.001 \). From Ommen et al,15 with permission from the publisher. Copyright © 2005, the American College of Cardiology Foundation.
sible to arbitrarily proclaim alcohol ablation to be the “new gold standard for the 21st century” or, remarkably, to argue that myectomy represents an impediment to the development of alcohol ablation.

**Technical Considerations**

Unlike alcohol ablation, for which precise targeting of the septum may be constrained by the size and distribution of septal perforator coronary arteries, the flexibility afforded the surgeon by direct visual inspection permits recognition of all morphological abnormalities that contribute to mechanical LV outflow obstruction. These include inhomogeneous thickness of the septum (Figure 4) and papillary muscle anomalies such as direct insertion into anterior mitral leaflet (Figure 5). In addition, recognition that greatly elongated mitral valve leaflets can produce obstruction (even after adequate myectomy) has led to valve repair or plication in some cases. Myectomy avoids mitral valve replacement and can be regarded as a “pure” intervention, rarely leaving behind implanted devices (pacemakers and defibrillators) and never potentially arrhythmogenic myocardial scarring. The complexity and heterogeneity of outflow tract morphology (and necessity for the transaortic approach) have formulated the customary recommendation that septal myectomy be performed by surgeons having specific experience with this operation and HCM.

**Alcohol Septal Ablation**

**Historical Context**

Despite the known benefits of myectomy, it has historically been an aspiration in HCM to develop alternative treatment strategies for operative candidates with obstacles to low-risk surgery (eg, obesity, important comorbidity, particularly advanced age, or insufficient motivation for surgery). In the early 1990s, dual-chamber pacing was promoted as an alternative (or replacement) for surgery but proved less effective than myectomy, and in randomized trials, perceived clinical benefit represented only a placebo effect.

In 1995, Dr Ulrich Sigwart applied percutaneous methodology to HCM in which 2 to 4 cm³ of 96% ethanol is introduced into a septal perforator branch of the left anterior descending coronary artery (often guided by myocardial contrast echocardiography) to intentionally produce an infarction in the ventricular septum. After a transient drop in gradient as a result of stunning, ultimate resolution of obstruction requires several months of septal remodeling, leading to outflow tract widening and reduced mitral valve systolic anterior motion (ie, in effect mimicking the pathophysiology of myectomy).

**Clinical Results**

Results of alcohol ablation (Table 2) have now been documented in numerous short-term observational studies (average follow-up, ~0.5 to 3 years). Ablation reduces LV outflow obstruction, although on average somewhat less than myectomy (residual rest gradient, 20 to 25 versus 0 to 10 mm Hg for surgery). Improvements in symptoms and exercise capacity may occur, according to...
the principle that interventions that relieve outflow gradient in HCM will likely improve heart failure symptoms. However, treatment failures have been reported in a substantial minority of patients (ie, up to 25%) (Figure 6), particularly in those with large outflow gradients; induced complete heart block requiring permanent pacemaker dependency occurs in 5% to 33% of patients.

Emergence and Concerns

Over the last 7 years, enthusiasm for alcohol septal ablation has accelerated exponentially, with this technology now considered part of routine interventional practice. Interest in ablation has seemed unbridled, instinctually driven by the erroneous assumption that contemporary and percutaneous (“nonsurgical”) strategies are always implicitly more benign and advantageous than traditional open heart surgery. Indeed, there have been more alcohol septal ablation procedures (estimated 5000) performed in the last 5 to 7 years than myectomies in 45 years; overall, most septal reduction interventions for obstructive HCM are now probably alcohol ablations.

But do these developments in management strategy really serve the best interests of the HCM patient population? First, the disproportionate number of percutaneous versus surgical procedures is a legitimate concern, given that the professed clinical threshold (ie, magnitude of symptoms and gradient) professed for both treatments is identical. Consequently, it is an inescapable conclusion that less stringent patient selection criteria are used for alcohol ablation than for surgery, with many patients undergoing ablation prematurely (often with only mild symptoms after less than maximal medical management). Of note, over the past 14 years, only 5% of my large HCM cohort have required referral for either surgery or ablation.

Second, we have witnessed virtual elimination of myectomy in several European countries (eg, Germany, Switzerland) and some respected centers in the United States (eg, Stanford), all formerly strong proponents of surgical management. In such clinical settings, myectomy has been relegated to the challenging task of relieving obstruction after a failed ablation (and in the presence of large septal scars), a circumstance that also results in pacemaker dependency and may be associated with more complicated technical considerations and hospital course. Certainly, the loss of myectomy expertise for a generation of cardiac surgeons cannot be viewed as advantageous for the future management of HCM. On the other hand, interventional alcohol ablation has been widely criticized for its failure to establish formal rigorous training and to define acceptable levels of expertise.

Third, interest in alcohol ablation as a novel treatment strategy has created a virtual flood of observational studies (often published with priority) from a variety of clinical laboratories. This skewing of the recent literature has been so pervasive that it is likely that many newly trained cardiolo-
gists may not even be fully aware of the surgical option (Table 3). In addition, it is worth citing certain specific limitations of the available ablation literature, including incomplete patient follow-up in some reports, underreporting of complications and death rates in inexperienced interventional laboratories sporadically performing ablation, and the unfortunate forced retraction of a major ablation article from a highly respected medical journal.

### TABLE 2. Advantages and Disadvantages of Alcohol Septal Ablation

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Disadvantages</th>
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<tbody>
<tr>
<td>Percutaneous technique (does not require surgeon, cardiopulmonary bypass, or open heart operation)</td>
<td>Procedural mortality not insignificant</td>
</tr>
<tr>
<td>Short in-hospital stay</td>
<td>Produces large, transmural infarct with arrhythmogenic potential and possible increased sudden death risk</td>
</tr>
<tr>
<td></td>
<td>Inflexible; confined to anatomic distribution of septal perforator artery, cannot be tailored to complex LVOT anatomy</td>
</tr>
<tr>
<td></td>
<td>Not infrequently associated with CHB requiring permanent pacemaker</td>
</tr>
<tr>
<td></td>
<td>Defibrillator implantation not uncommon because of heightened sudden death risk</td>
</tr>
<tr>
<td></td>
<td>Not infrequently requires repeated interventions</td>
</tr>
<tr>
<td></td>
<td>Relief of gradient not immediate, requiring several weeks to fully evolve</td>
</tr>
<tr>
<td></td>
<td>Often ineffective in patients with highest gradients</td>
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</tbody>
</table>

CHB indicates complete heart block; LVOT, LV outflow tract.

### Clinical Implications of the Scar

A major and largely unresolved issue connected to septal ablation relates to the potential long-term consequences of alcohol-induced necrosis and myocardial infarction as an arrhythmogenic substrate that predisposes susceptible patients to lethal reentrant ventricular tachyarrhythmias. This is not an idle consideration that can be easily dismissed, given that HCM is the most common cause of sudden death in young people.

Some observers have suggested that the alcohol-induced scar does not represent a true infarction because of its

### TABLE 3. Popular Misconceptions, Myths, Rationalizations, and Excuses Used to Ignore Surgical Myectomy for Patients With Obstructive HCM

I do not believe in surgery.
Surgical risk is too high.
Do they really do surgery for HCM anymore?
You do not hear much about surgery.
You hear a lot more about alcohol ablation now.
Our surgeons are afraid (or refuse) to do a myectomy.
Our surgeon has never done a myectomy.
We just cannot send all these patients out to Mayo for surgery.
We do alcohol ablation first and, if unsuccessful, then another ablation, and then maybe transplant. What else is there?
Myectomy causes dilated cardiomyopathy and leads to heart transplant.
Alcohol septal ablation is safe and benign, not like surgery.
Why would anyone have surgery if he or she had a choice?
Surgery also produces an infarct just like ablation.
Ablation must be better than surgery because it is newer.

*As actually told to the author by cardiologists, 2004 to 2006.*
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established,39,42,81–87 (ie, at a rate of 8% per year,86,87 and with ablation-related events do frequently occur is now well extended follow-up studies. However, the fact that such arrhythmias continue after alcohol ablation is unresolved and requires greatly increased enthusiasm for prophylactic defibrillator implantation after ablation.83,85–87 Therefore, unlike myectomy, it is possible that alcohol-imposed infarcts could act as a new HCM risk factor, compounding the underlying myocardial electric instability already present in some patients, for whom unpredictable sudden death risk is known to extend over many decades.3,4,83,88 Consequently, for some patients, alcohol ablation could represent an unfavorable net tradeoff of gradient relief for increased arrhythmia risk.

Indeed, alcohol ablation is unique among cardiovascular treatment strategies by aspiring to hemodynamic benefit via destruction of myocardial tissue and, in the process, contradicting a major tenet of preventive cardiology, to minimize the likelihood of infarction and scarring. Recently introduced experimental septal reduction interventions, which circumvent surgery and ablation (eg, coil embolization, stenting, radiofrequency ablation), also impose sizable septal infarctions similar to those incurred with alcohol.89–92 Finally, early experience suggests that myectomy performed after failed alcohol septal ablation may be associated with more complicated technical considerations and hospital course.

Considerations for late postprocedural arrhythmias have led to the prudent recommendation that alcohol ablation should be confined largely to adults of relatively advanced age in whom the potential risk period is shortest.3,4,11,51,74–76 Although some practitioners have inadvisably lowered the age of acceptability for ablation well into childhood85,72,89,93 (remarkably, to ages as young as 3 and 5 years),89,93 it is the prevailing view of HCM experts that alcohol septal ablation should be strongly discouraged in children, adolescents, and young adults.3

Another unfortunate byproduct of this controversy and the euphoria associated with relieving obstruction with alcohol ablation is the misconception that LV outflow gradients (traditionally, a highly visible feature of HCM) are always the predominant clinical facet of this complex disease. As a consequence, other important issues such as risk stratification for sudden death, family screening, and genetic counseling may not always receive the attention they deserve.

**Patient Autonomy and the “Gatekeeper” Effect**

The rapid penetration of alcohol ablation into cardiology practice has often been associated with preferential referral for this procedure without the explicit presentation of other available treatment options (ie, surgical myectomy). This strategy represents an ethical dilemma and, in effect, violates the important principle of patient autonomy (ie, that patients possess a fundamental right to full disclosure of all medical information that may potentially affect their health, safety, and risk for death or injury, as well as an opportunity to actively participate in treatment decisions that dictate their medical destiny) (Table 3). Similar considerations triggered the recent Guidant Affair, in which industry executives withheld from patients and their physicians crucial information about defective implantable defibrillators, known only by the corporation to be unreliable in preventing sudden death.94

Cardiologists in the role of gatekeeper bear a similar responsibility with respect to ablation and myectomy: to fully inform patients on the advantages and disadvantages of both septal reduction treatments (Table 3). If patients are not fully apprised of all therapeutic options, they are, in effect, deprived of the opportunity to formulate truly informed decisions. Indeed, this is a fundamental premise of those specialty centers of excellence focused on the diagnosis and management of HCM (where both expert surgery and ablation are available). Finally, recognition that the patient autonomy principle applies to decisions about ablation or surgery requires a willingness to override the inherent resistance to
referring patients out of institutions and networks that lack accomplished myectomy surgeons (to those that do) when this strategy represents a clear benefit to patients. Such recommendations for HCM are not unlike those made by an American College of Cardiology/American Heart Association consensus panel regarding preferential patient referral for mitral valve repair to centers experienced with that particular operation.55

Final Thoughts
The central issue in the current myectomy versus ablation debate resides with proper patient selection. The American College of Cardiology/European Society of Cardiology expert panel recently commissioned to establish consensus guidelines for the management of HCM (including practitioners of surgery and ablation),2 and unfortunately largely ignored by the interventional community, formally advocated septal myectomy as the primary treatment option for disabling drug-refractory heart failure symptoms resulting from outflow obstruction. Alcohol septal ablation is regarded as an important but nevertheless alternative intervention for selected patients who are not optimal surgical candidates. Because a prospective randomized trial comparing alcohol ablation and myectomy is impractical and unlikely to occur to resolve this debate,96 there is little reason to look beyond the more-established surgical myectomy as the first option for most patients.

Alcohol ablation has been heavily promoted by interventional cardiology over the last several years,33,34,39,41–45,63 but now it is imperative that the pendulum swing back toward surgery.11,51 Indeed, there does not appear to be a compelling reason to aggressively advance a new invasive treatment option for obstructive HCM (ie, alcohol ablation) that may result in pacemaker and defibrillator dependency, increase the risk for late sudden death, incur potential complications from the implanted devices, and convey a not-inconsequential procedural mortality rate. This is particularly true when an established and time-honored intervention (surgical myectomy) is available that has already served this patient population exceptionally well for >45 years by virtue of extremely low operative risk, more consistent amelioration of symptoms resulting from permanent relief of mechanical impedance to LV outflow, and a documented survival benefit affording the opportunity to achieve normal life expectancy.

Disclosures
None.

References


I have the highest regard for Dr Maron’s unsurpassed experience and expertise in hypertrophic cardiomyopathy. I agree with him that the principle of patient autonomy requires that cardiologists fully inform patients about all treatment options, but I feel obliged to point out that we must compare apples to apples. It is not appropriate to compare the apples of idealized septal myectomy outcomes reported from a very few centers, beginning after the steep portions of practitioners’ learning curves and omitting patients undergoing concomitant cardiac surgery, to the oranges of actual septal ablation outcomes reported from the very early experience with the procedure. It would be misleading to equate the highly selected surgical mortality figures chosen by Dr Maron with those of patients in actual clinical practice. The mortality rate of septal myectomy is not zero! Furthermore, the need for postmyectomy permanent device therapy arises more than rarely, and we as well as others have performed septal ablation in patients who had undergone unsuccessful septal myectomy. The theoretical concern that septal ablation would increase the incidence of fatal arrhythmias has fortunately not been realized; indeed, the publication of Lawrenz et al cited by Dr Maron is actually entitled “Transcoronary Ablation of Septal Hypertrophy Does Not Alter ICD Intervention Rates in High-Risk Patients With Hypertrophic Obstructive Cardiomyopathy.” I agree with Dr Maron that patients should undergo septal reduction therapy only after truly optimal medical therapy has failed, following a balanced and dispassionate presentation of the treatment options and in the context of comprehensive management of their disease.
Most Fully Informed Patients Choose Septal Ablation Over Septal Myectomy

Michael A. Fifer, MD

Hypertrophic cardiomyopathy (HCM) is a disease characterized by primary hypertrophy of the left (and sometimes right) ventricle. The clinical manifestations of the disease are dyspnea, angina, and a continuum encompassing lightheadedness, presyncope, syncope, and sudden death. Although HCM often is caused by an identifiable mutation in a gene coding for a sarcomeric protein and inherited in an autosomal-dominant pattern, many patients do not have any relatives in whom the disease is manifest. The prevalence of HCM is estimated to be 0.2%, with ~600 000 Americans affected.

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Several anatomic variants of HCM exist. Of these, hypertrophic obstructive cardiomyopathy (HOCM) is the variant that has been the subject of the most intense investigation. HOCM was previously termed idiopathic hypertrophic subaortic stenosis and is characterized by 4 closely related pathoanatomic features (Figure 1).\(^1\) Obstruction to left ventricular (LV) outflow is caused by bulging of the thickened septum into the left ventricular outflow tract (LVOT) during systole, with apposition of the anterior (occasionally posterior) leaflet of the mitral valve, which demonstrates systolic anterior motion. Mitral regurgitation usually is present, although the degree varies greatly among patients with HOCM. LVOT gradients may be present at rest or only during Valsalva maneuver or exercise (provocable obstruction). A recent report suggests that if patients with provocable gradients are included, most patients with HCM have the obstructive form of the disease.\(^2\)

Management of HCM

The management of HCM may be considered as consisting of 4 elements (Table 1).\(^3\) For patients at high risk of sudden death, implantation of a cardioverter–defibrillator is considered.\(^4\) In patients with HOCM, the first line of therapy for symptoms consists of medications with negative inotropic properties that diminish the extent of septal bulging into the LVOT; these are \(\beta\)-blockers, calcium channel blockers (of which there has been the largest experience with verapamil), and disopyramide. In most patients, symptoms can be adequately controlled with these medications used alone or in combination. In patients with HOCM and symptoms refractory to optimal medical therapy, mechanical measures aimed at relief of the outflow tract obstruction are considered.

Septal Myectomy

The original mechanical management of patients with HOCM and refractory symptoms consisted of septal myotomy, or
simple incision of septal muscle, first performed in 1958.\(^5\),\(^6\) Myotomy was soon replaced by septal myectomy, or removal of septal muscle.\(^7\),\(^8\) In this approach, the surgeon visualizes the thickened septum through an incision in the aortic root and excises a rectangular segment from the basal septum toward the apex. In patients with septal thickness 15 to 18 mm, septal myectomy incurs a risk of causing a ventricular septal defect; in these cases, an alternative strategy is repair or replacement of the other structure implicated in LVOT obstruction, namely the mitral valve.

### Pacing

Dual-chamber pacing with a short atrioventricular delay was suggested as early as 1968 as an innovative approach for the management of HOCM.\(^9\) Although marked beneficial effects of pacing were reported in uncontrolled series,\(^10\) these findings have not been reproduced in randomized controlled trials,\(^11\),\(^12\) although a suggestion exists that a small subset of patients benefits from pacing.\(^12\)

### Septal Ablation

Transcatheter ablation of the septum with ethanol was first performed at the Royal Brompton Hospital in London in 1994.\(^13\),\(^14\) The first patient to undergo septal ablation had severe symptoms despite \(\beta\)-blockade and a resting gradient of 25 mm Hg that increased markedly during the Valsalva maneuver. Peak creatine kinase was 2500 U/L. She was discharged 3 days after septal ablation and was asymptomatic 10 months later. The results were similar for the other 2 patients in the initial report, both of whom also had LVOT gradients that were low at rest and higher in response to provocative maneuvers.

Because the proximal septal branches of the left anterior descending coronary artery supply the conduction system as well as the basal septum, atrioventricular block is a common complication of septal ablation. For this reason, a temporary pacemaker is placed before the procedure. With standard coronary angioplasty guiding catheters, guidewires, and balloon catheters, the most proximal septal branch that can be catheterized is entered, and the angioplasty balloon is inflated. X-ray contrast is injected through the balloon catheter to confirm filling of the septal branch and absence of backflow into the left anterior descending coronary artery itself. Correct catheter placement also is confirmed by myocardial contrast echocardiography (see below). Dehydrated ethanol, usually 1 mL at a time, is then injected slowly through the balloon catheter, causing a targeted myocardial infarction; the usual total dosage of ethanol is 1 to 3 mL. Patients receive narcotics and experience mild to moderate chest pain, usually burning in quality. The gradient can usually be reduced to <20 mm Hg (Figure 2). In some cases, ethanol is injected selectively into septal subbranches\(^15\); in others, it is injected into 2 or 3 septal branches. After delivery of ethanol, distal flow in the affected septal branch is slow or absent (no-reflow phenomenon; see Figure 3).\(^16\)

Myocardial contrast echocardiography was introduced into the procedure to localize the septal branch supplying the critical septal segment (ie, the point of mitral valve contact and maximal flow acceleration).\(^17\),\(^18\) Myocardial contrast may

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**TABLE 1. Elements of the Management of HCM**

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<tr>
<td>Screen first-degree relatives for HCM</td>
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<tr>
<td>Avoid strenuous exertion, especially burst activity and isometric exercise, and volume depletion</td>
</tr>
<tr>
<td>Control symptoms</td>
</tr>
<tr>
<td>Assess risk for and prevent sudden death</td>
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</tbody>
</table>

Adapted from Binder et al\(^3\) with permission of the publisher. Copyright © 2005, The Massachusetts Medical Society.
be achieved with agitated x-ray contrast or an echocardiographic contrast agent. Myocardial contrast echocardiography may identify inappropriate sites for injection of ethanol such as a septal branch supplying myocardium too close to the apex, papillary muscle, inferoposterior LV, or right ventricle. Incorporation of this technique reduces the number of septal branches into which ethanol is injected and may both improve success rate and lower marker release and the need for pacing.17,19

Peak creatine kinase is \( \approx 500 \text{ U/L per 1 mL ethanol injected} \). In patients with failed septal ablation who subsequently undergo septal myectomy, we have found pathological evidence of necrosis of the vascular endothelium (Figure 4), suggesting that ethanol is toxic to both the coronary circulation and the myocardium.16

**What Do We Know About the Efficacy and Safety of Septal Myectomy?**

Septal myectomy performed by skilled surgeons at high-volume centers results in abolition of the LVOT gradient and relief of symptoms in the great majority of cases (Table 2).20–23 Results in patients with provokable obstruction are comparable to those in patients with resting obstruction.20 Early mortality, which was high in the early experience with this operation, has been reduced to \( \leq 2\% \) in young or middle-aged otherwise healthy patients undergoing isolated septal myectomy. In older patients, those with comorbid conditions, and those requiring other concomitant cardiac surgery, mortality is considerably higher.22,24,25

Complications of septal myectomy include those peculiar to the operation (eg, ventricular septal defect [1%]20,26 and complete heart block for which a permanent pacemaker is required [3% to 10%, lower in the absence of preexisting conduction system disease]).20–22,26 and those that pertain to any cardiac operation (eg, postoperative bleeding with tamponade, sepsis, and stroke).20–22 Postoperative left bundle-branch block occurs in 40% to 56% of patients.24,26,27 When septal myectomy is successful and uncomplicated, studies with a mean follow-up of 6 to 12 years indicate that the improvement is usually sustained.20–22,25,26 Successful septal myectomy results in a decrease in LV mass that is much greater than that attributable to the removal of the septal myocardium itself and that undoubtedly results from relief of pressure overload.28

**What Do We Know About the Efficacy and Safety of Septal Ablation?**

Septal ablation performed by skilled operators at high-volume centers results in a marked immediate decrease in LVOT gradient in the great majority of patients.17,29–32 In a sizable subset of patients, the gradient response is triphasic, with immediate reduction, early reappearance, and by 3 months after the procedure, sustained fall.33,34 This sequence suggests that myocardial stunning may be responsible in large part for the immediate reduction in gradient. After recovery from stunning, ultimate gradient reduction is associated with remodeling of the septum with an increase in LVOT area.35 Improvement in symptoms occurs over the same 3-month period. Symptom relief and gradient reduction are achieved in \( >80\% \) of patients (Table 3).32,36,37 A clinical impression exists that patients with septal thickness approaching or exceeding 30 mm may not achieve full benefit from septal ablation.

In association with the amelioration of the LVOT gradient, the degree of mitral regurgitation decreases,17,29,38 as does the size of the left atrium.17,39 In response to a reduction in the systolic pressure load, systolic myocardial function improves
in the free wall and hypertrophy regresses throughout the LV (as after aortic valve replacement for aortic stenosis; Figure 5). Reduction in LVOT gradient and regression of LV hypertrophy are accompanied by improvement in diastolic LV function, which correlates with an increase in exercise capacity.

Two studies have demonstrated that, as with septal myectomy, the benefit of septal ablation in patients with provokable gradients is similar to that in patients with resting gradients. These studies provide retrospective support for Sigwart’s performance of septal ablation in his first 3 patients, all of whom had provokable obstruction. The standard provocation for deciding whether a patient is a candidate for septal ablation is exercise. Because exercise is not practical in an instrumented patient, patients triaged to ablation on the basis of exercise-induced gradients may receive dobutamine or isoproterenol during the procedure to provide a gradient suitable to serve as a “target” for ablation.

Temporary complete atrioventricular block occurs during the procedure in approximately half of the patients. After the procedure, right bundle-branch block is present in approximately half of the patients. A corollary is that patients with preexisting left bundle-branch block usually require permanent pacing after ablation. Another corollary is that patients who undergo sequential septal ablation and septal myectomy (which frequently causes left bundle-branch block) also are likely to require permanent pacing. Although the rate of permanent pacemaker placement was as high as 38% early in the septal ablation experience, it has fallen with the introduction of myocardial contrast echocardiography and the use of lower dosages of ethanol, with 1 group reporting an incidence of <10%,.

In-hospital mortality is 0% to 4%. Deaths have been due to coronary dissection, pulmonary embolism, refractory ventricular fibrillation, right ventricular perforation by the temporary pacemaker, pump failure, and heart block. In-hospital sustained ventricular tachyarrhythmias occur in 5% of cases. The theoretical concern that after septal ablation, arrhythmic sudden death resulting from superimposition of a myocardial infarction on a cardiomyopathic substrate would be common has fortunately not been realized in clinical practice. In patients with preexisting risk factors for sudden death, an implantable cardioverter–defibrillator may be placed before septal ablation.

Other complications of the procedure are remote myocardial infarction caused by aberrant ethanol injection or collateral circulation and ventricular septal rupture. Because of the latter potential complication, septal ablation should not be performed if septal thickness at the site of planned ethanol delivery is <15 mm.

Comparison of Septal Ablation and Septal Myectomy

There have been no prospective randomized trials comparing septal ablation with septal myectomy. Investigators have compared the results of septal ablation with those of septal myectomy in several nonrandomized studies (Table 4).

### TABLE 2. Results of Septal Myectomy

<table>
<thead>
<tr>
<th>Authors</th>
<th>Institution</th>
<th>No.</th>
<th>Early Mortality, %</th>
<th>PPM Rate, %</th>
<th>NYHA Class, %</th>
<th>Late Survival, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heric et al</td>
<td>Cleveland Clinic</td>
<td>178</td>
<td>6</td>
<td>4</td>
<td>10</td>
<td>71 23 NA 86 70</td>
</tr>
<tr>
<td>Robbins and Stinson</td>
<td>Stanford</td>
<td>158</td>
<td>3</td>
<td>2</td>
<td>3</td>
<td>NA NA 92 85 71</td>
</tr>
<tr>
<td>Wu et al</td>
<td>Toronto General Hospital</td>
<td>338</td>
<td>1.5</td>
<td>0.8</td>
<td>6</td>
<td>98 Combined 98 95 83</td>
</tr>
<tr>
<td>Ommen et al</td>
<td>Mayo Clinic</td>
<td>289</td>
<td>NA</td>
<td>0.7</td>
<td>1.0</td>
<td>88 Combined 98 96 83</td>
</tr>
</tbody>
</table>

PPM indicates permanent pacemaker; NA, not applicable.

### TABLE 3. Results of Septal Ablation

<table>
<thead>
<tr>
<th>Authors</th>
<th>Institution</th>
<th>No.</th>
<th>Early Mortality, %</th>
<th>PPM Rate, %</th>
<th>Follow-Up, mo</th>
<th>NYHA Class, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gietzen et al</td>
<td>Bielefeld</td>
<td>157</td>
<td>2.5</td>
<td>25</td>
<td>10±8</td>
<td>55 40</td>
</tr>
<tr>
<td>Fernandes et al</td>
<td>Baylor</td>
<td>130</td>
<td>1.5</td>
<td>13</td>
<td>43±14</td>
<td>79 NA</td>
</tr>
<tr>
<td>Faber et al</td>
<td>German registry</td>
<td>242</td>
<td>1.2</td>
<td>9.6</td>
<td>5±2</td>
<td>47 41</td>
</tr>
</tbody>
</table>

PPM indicates permanent pacemaker; NA, not applicable.
In an institution at which both procedures were regularly performed, patients were triaged according to clinical factors, so the groups were not comparable. In particular, the 25 patients undergoing septal ablation were older and had a higher prevalence of comorbid conditions than did the 26 patients undergoing myectomy. At the 3-month follow-up, the gradient reduction was more complete in the surgical cohort, whereas the 2 groups had similar reductions in symptoms, septal thickness, and degree of mitral regurgitation. No deaths occurred in either group.

In the second study from 2 hospitals that each favored 1 of the procedures, patients were triaged according to institutional preference. In this study, it was possible to match patients for age and LVOT gradient. Forty-one patients were included in each group. At the 1-year follow-up, severity of symptoms, maximal oxygen uptake, LVOT gradient, septal thickness, and degree of mitral regurgitation were similar for the 2 therapies. There was 1 death during septal ablation as a result of coronary dissection.

A third study compared the effects of septal ablation in 20 patients with those of septal myectomy in 24 patients. Patients who underwent myectomy were younger than those who had ablation. There was 1 death in each group. Although improvements in LVOT gradient and New York Heart Association (NYHA) class were similar in the 2 groups, the increase in maximal oxygen uptake was higher in the patients who underwent surgery.

In a fourth study, patients were triaged to ablation or surgery on the basis of age and other clinical factors. The outcomes of 54 patients undergoing septal ablation were compared with those of 48 patients undergoing septal myectomy. Relief of symptoms was more complete in the surgical group. More late deaths occurred in the ablation group.

A comparison of echocardiographic indexes of diastolic function an average of 5 months after intervention demonstrated no difference between septal ablation and septal myectomy.

**Which Patients Are Candidates for Mechanical Therapy for HOCM?**

Mechanical therapy is appropriate for patients with HOCM who have symptoms (exertional dyspnea, angina, and/or “hemodynamic” syncope) that interfere significantly with lifestyle and are refractory to optimal medical therapy. The clinical threshold for performing septal ablation should be identical to that for performing septal myectomy.

Optimal therapy consists of β-blockade titrated to symptom relief, heart rate, or an adverse reaction. In patients with substantial symptoms despite optimal β-blockade, disopyramide, starting as 150 mg BID in the controlled-release form, may be added. Although disopyramide administration is sometimes limited by QT prolongation, a retrospective mul-

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**TABLE 4. Studies Comparing Septal Ablation With Septal Myectomy**

<table>
<thead>
<tr>
<th>Authors</th>
<th>Institution(s)</th>
<th>Ablations, n</th>
<th>Myectomies, n</th>
<th>How Triaged</th>
<th>Efficacy</th>
<th>Safety</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nagueh et al</td>
<td>Baylor (ablation), Mayo Clinic (myectomy)</td>
<td>41</td>
<td>41</td>
<td>Institutional preference</td>
<td>No difference in NYHA class, exercise capacity, or gradient</td>
<td>Death in 2% ablation vs 0% myectomy; PPM in 22% ablation vs 2% surgery</td>
</tr>
<tr>
<td>Qin et al</td>
<td>Cleveland Clinic</td>
<td>25</td>
<td>26</td>
<td>Age, comorbid conditions, need for concomitant surgery</td>
<td>No difference in NYHA class; &gt;50% gradient reduction in 76% ablation vs 100% myectomy</td>
<td>No deaths; PPM in 24% ablation vs 8% myectomy</td>
</tr>
<tr>
<td>Firoozi et al</td>
<td>St. George's Hospital</td>
<td>20</td>
<td>24</td>
<td>Age, patient and physician choice</td>
<td>No difference in NYHA class or gradient; exercise capacity better after myectomy</td>
<td>Death in 5% ablation vs 4% myectomy; PPM in 15% ablation vs 4% myectomy</td>
</tr>
<tr>
<td>Ralph-Edwards et al</td>
<td>Toronto General Hospital</td>
<td>54</td>
<td>48</td>
<td>Age, patient and physician choice</td>
<td>NYHA class I or II in 41% ablation vs 72% myectomy</td>
<td>Late death in 11% ablation vs 0% myectomy</td>
</tr>
</tbody>
</table>

PPM indicates permanent pacemaker.
ticenter study provides some evidence against a proarrhythmic effect of the drug in patients with HOCM. In patients with noncardiac side effects of β-blockade, verapamil usually is substituted.

In patients without resting LVOT gradients of at least 30 to 50 mm Hg, exercise may bring out a provokable gradient. Patients with obstruction at rest or during exercise are candidates for mechanical therapy if they have symptoms that interfere substantially with their lifestyles despite truly optimal medical therapy. Published guidelines suggest that patients undergoing mechanical therapy should be in NYHA class III or IV. Because patients in NYHA class II have, by definition, symptoms during ordinary physical activity, some of these patients also are appropriate candidates for either septal ablation or septal myectomy. Patients in class II are, in fact, often managed with either septal ablation or septal myectomy. On the other hand, some patients in NYHA class III choose to live with their symptoms rather than undergo interventional or surgical management.

Retrospective studies have suggested that prognosis in HCM is related to the presence of a resting LVOT gradient and that prognosis in HOCM is favorably affected by septal myectomy. In the absence of conclusive prospective data to indicate that reducing or abolishing the gradient improves prognosis, however, mechanical therapy should not be offered to patients, even those with large gradients, if they have no or mild symptoms.

In some cases, HOCM is associated with intrinsic abnormalities of the mitral valve. These and other patients who require concomitant valve surgery or coronary bypass grafting should undergo septal myectomy rather than septal ablation. Surgery also should be considered for patients with atrial fibrillation who might benefit from a concomitant maze procedure.

**Advantages of Septal Myectomy**

1. The success rate for septal myectomy is higher than that for septal ablation. This difference results in part from the dependence of the septal ablation procedure on the vagaries of septal anatomy.
2. Sustained relief of outflow obstruction occurs immediately after septal myectomy but may be delayed by up to 3 months after septal ablation.
3. Longer-term data are available for septal myectomy than for septal ablation, a consideration of particular relevance to the management of younger patients.
4. Although both septal myectomy after failed septal ablation and septal ablation after failed septal myectomy have been carried out successfully, the former is more common. Because septal ablation often causes right bundle-branch block and septal myectomy often causes left bundle-branch block, patients undergoing the 2 procedures in sequence incur a very high risk of complete heart block, necessitating permanent pacing. A younger patient may therefore be better served by the strategy of primary septal myectomy to avoid the prospect of decades of permanent pacing.

**Advantages of Septal Ablation**

1. Septal ablation has the potential for greater patient satisfaction because of absence of a surgical incision and need for general anesthesia, the lower amount of pain, and the much shorter recovery time.
2. The benefit of alcohol septal ablation in older patients is similar to that in younger patients. Because the risks of cardiac surgery, particularly stroke, increase with age, ablation may offer an advantage in older patients.
3. The cost of septal ablation is less than that of septal myectomy.

**What We Do Not Know**

1. No randomized trials have been conducted on septal ablation versus septal myectomy.
2. Conclusive data on the effect of either septal ablation or septal myectomy on life expectancy are not available.
3. Although it is clear that life-threatening ventricular tachyarrhythmias after septal ablation are rare, they have been reported in sporadic cases. In the absence of definitive data, a reasonable strategy is to consider septal ablation a potential risk factor for sudden death. A corollary is that patients with preexisting risk factors (recurrent syncope, family history of sudden death in association with HCM, ventricular tachycardia, severe hypertrophy, or abnormal blood pressure response to exercise) should be considered for implantation of a cardioverter–defibrillator before septal ablation.
4. The first septal ablation was performed in 1994; thus, long-term follow-up data in substantial numbers of patients are not available.
5. Studies comparing the cost-effectiveness of septal ablation and septal myectomy have not been done.
6. It is not known whether the outcomes of septal ablation and septal myectomy described at high-volume centers can be reproduced at other institutions.

Thus, although some have expressed strong, well-reasoned opinions in support of either septal ablation or septal myectomy as the procedure of choice, existing data are inconclusive, so the management decision in many cases depends critically on patient choice.

**Application to Patient Care**

Triage of patients to septal ablation or septal myectomy is illustrated by the following recent real-life cases from Massachusetts General Hospital.

Case 1: A 43-year–old man had exertional dyspnea and angina despite β-blockade. Septal thickness was 16 mm, and LVOT gradient 72 mm Hg. On the combination of a β-blocker and disopyramide, his symptoms remitted.
Case 2: A 61-year–old man had severe lightheadedness and exertional dyspnea despite optimal medical therapy in association with HOCM and pulmonary fibrosis. Septal thickness was 22 mm, and LVOT gradient 116 mm Hg. Because of his pulmonary disease, the patient underwent septal ablation.

Case 3: A 27-year–old man had presyncope and progressive exertional angina and dyspnea despite optimal medical therapy. Septal thickness was 26 mm, and LVOT gradient 184 mm Hg. His symptoms were refractory to medical therapy. Because of his young age and marked hypertrophy, the patient underwent septal myectomy.

Case 4: A 73-year–old woman had severe bisidet heart failure in association with HOCM and chronic obstructive pulmonary disease. Septal thickness was 24 mm, and LVOT gradient 121 mm Hg. Diuresis was limited by hypotension and azotemia. Because she was in need of immediate relief of outflow obstruction and despite her concomitant pulmonary disease, the patient underwent septal myectomy.

Case 5: A 46-year–old woman had disabling angina, dyspnea, and lightheadedness despite optimal medical therapy. Septal thickness was 19 mm, and LVOT gradient 121 mm Hg. Both mechanical options—septal ablation and septal myectomy—were offered to the patient.

For patients like the last one, clinical decision making is not informed by clear-cut data demonstrating that either septal ablation or septal myectomy is superior. For such “gray-area” patients, the principle of patient autonomy dictates that it is appropriate for the properly informed patient to choose between the 2 procedures.

What to Tell Patients

Patients’ decisions depend critically on the information given to them by their physicians and the manner in which it is presented. To enable the patient to make what for him or her is the best decision, the physician must present a thorough and objective comparison of the 2 procedures. The physician must recognize that local outcomes for either septal ablation or septal myectomy may not match those from high-volume centers. For example, the incidence of heart block for which permanent pacing is indicated may be higher for both procedures than that reported from a few select centers. All percentage estimates should be modified accordingly. Representative considerations to communicate to patients are the following:

1. The medium-term success rate for septal myectomy (≈90% to 95%) is higher than that for septal ablation (≈80% to 90%).
2. Clinical benefit is realized immediately after recovery from septal myectomy but may be delayed for up to 3 months after septal ablation.
3. Neither the long-term success rate for septal ablation nor the long-term consequences of the septal ablation scar is known.
4. The mortality rates of the 2 procedures (in otherwise healthy patients) are comparable (≈1% to 2%).
5. The chance of needing a permanent pacemaker is much higher after septal ablation (≈10% to 15%) than after septal myectomy (≈5%).
6. Although it is possible to have septal myectomy after failed septal ablation, the likelihood of needing a permanent pacemaker is extremely high after that sequence.
7. In older patients, the chance of having a stroke is lower with septal ablation than with septal myectomy.
8. The recovery time after septal myectomy is much longer than that after septal ablation.

What Patients Will Choose

Cardiologists and their patients are confronted by the choice between percutaneous transcatheter and surgical therapies much more often in coronary artery disease than in HOCM. In the setting of coronary artery disease, most, but not all, patients for whom either procedure would be appropriate choose percutaneous coronary intervention over coronary artery bypass grafting. The choice appears to be motivated by substantial value placed by the patient in the avoidance of the incision, general anesthesia, pain, and/or long recovery associated with surgery. These factors also have engendered extension of nonsurgical interventional procedures to the management of congenital and valvular cardiac lesions.

Similarly, and for the same reasons, most gray-area patients with HOCM choose septal ablation over septal myectomy. Patients are of course influenced by the information presented to them by physicians. It is important to emphasize that not all patients fall into the gray area; as illustrated above by the case examples, many patients exist for whom the cardiologist should direct the management to either septal ablation or septal myectomy. It is also critical that gray-area patients be allowed to choose between the options in an unhurried, unpressured environment and to seek counsel from family, friends, other patients with HCM, and other physicians.

Conclusions

 Longer-term follow-up will permit judgment on the durability of the medium-term amelioration of LVOT gradient and improvement in symptoms observed in most patients after septal ablation. No data exist to support extending the current indications for mechanical management of HOCM to patients with only mild symptoms. If cardiologists adhere to strict inclusion criteria for septal ablation and septal myectomy, with either procedure performed only in patients with symptoms that interfere substantially with their lifestyles and are refractory to truly optimal (usually
2-drug) medical therapy, few centers offering the procedures are likely to maintain reasonable minimum case volumes. Operators performing the procedures at lower rates may have lower success and higher complication rates. Accordingly, performance of both septal ablation and septal myectomy should be confined to regional referral centers. The mechanical procedures should be offered only in the context of a program that integrates expertise in all aspects of HCM, including genetic counseling and arrhythmia management.

Future comparisons of the results of septal ablation and septal myectomy would be aided by adoption of a standard definition of success of the procedures. One possible definition would be improvement by ≥1 NYHA or Canadian Cardiovascular Society class and gradient reduction by ≥50% at 3 months after the procedure. Clinical equipoise would allow performance of a multicenter randomized trial comparing septal ablation and septal myectomy.62,63 Because mortality is low after both procedures, selection of a primary end point such as exercise capacity is advisable.

Acknowledgments

The author thanks Drs Igor F. Palacios, Michael H. Picard, and Gus J. Vlahakes for critically reviewing the manuscript.

Disclosures

Dr Fifer has received honoraria for speaking on HCM in general and on septal ablation in particular.

References


Dr Fifer has presented a reasonable portrayal of the surgery versus alcohol ablation controversy in obstructive hypertrophic cardiomyopathy (HCM), which at times has seemed much like a conflict between diametrically opposed forces of interventional cardiology and surgery. However, his title is revealing: “Most Fully Informed Patients Choose Septal Ablation Over Septal Myectomy.” Indeed, HCM experts believe patients often choose septal ablation because they are not fully informed as to these competing strategies. How else to reconcile Dr Fifer’s concession that myectomy is more successful than ablation and is associated with enhanced long-term survival equivalent to the general population? It is also gratifying that Dr Fifer recognizes ablation as a potential risk factor for sudden death due to the alcohol-induced transmural infarction. Nevertheless, a disappointing note is Dr Fifer’s perpetuation of the old unfortunate myth that procedural mortality is higher with myectomy than ablation, when he selectively cites outdated and 20-year–old surgical experiences irrelevant to current patients. Mortality is now lower with myectomy than ablation, even approaching zero at HCM centers. Similarly, Dr Fifer’s assertion that patients with only mild heart failure symptoms should be ablation candidates is unsettling. Here he appears to dispute and contradict the American College of Cardiology/European Society of Cardiology expert consensus recommendation that patients with severe unrelenting symptoms (class III) are most deserving of consideration for septal reduction, with myectomy usually the preferred option. We can all agree that fully informed patients and the principle of patient autonomy are critical. The anecdotal case reports from Dr Fifer’s institution seem very reasonable, but are they truly typical of the information provided most other HCM patients? The alcohol ablation euphoria argues that the myectomy option is not always presented accurately, a situation that has proved unfavorable to the best interests of HCM patients.
Most Fully Informed Patients Choose Septal Ablation Over Septal Myectomy
Michael A. Fifer

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