The Case for Surgery in Obstructive Hypertrophic Cardiomyopathy

Barry J. Maron, MD, FACC,* Joseph A. Dearani, MD,† Steve R. Ommen, MD, FACC,† Martin S. Maron, MD,‡ Hartzell V. Schaff, MD, FACC,† Bernard J. Gersh, MB, MBC1H, DP1II1, FACC,† Rick A. Nishimura, MD, FACC†

Minneapolis and Rochester, Minnesota; and Boston, Massachusetts

Relief of left ventricular (LV) outflow obstruction in patients with hypertrophic cardiomyopathy (HCM) and disabling symptoms refractory to maximum medical management has historically been a surgical problem. Surgical septal myectomy permanently abolishes systolic anterior motion of the mitral valve and mitral regurgitation, while normalizing LV pressures and wall stress. Also, these salutary goals are achieved without encumbering patients with post-procedural devices (e.g., pacemakers or defibrillators) or creating potentially arrhythmogenic substrates, as may occur with alcohol septal ablation. Procedural morbidity and mortality risk with myectomy is similar to, and in some institutions less than those for alcohol septal ablation. Over four decades, reports from numerous centers worldwide have consistently and unequivocally documented the benefits of surgery on hemodynamic and functional state, restoring normal and acceptable quality of life to patients of all ages by largely reversing the complications of heart failure. Long-term survival after myectomy is similar to that of the general population and superior to non-operated patients with obstruction. The LV outflow tract morphology in HCM is heterogeneous and not uncommonly includes congenital anomalies of the mitral valve apparatus for which the surgeon has the flexibility to adapt the repair, often employing an extended myectomy. In the current atmosphere of increasing and perhaps excessive enthusiasm for newer catheter-based interventions, it is a critical time to promote and re-emphasize that surgery is the time-honored (and presently the most effective) treatment strategy for relieving heart failure-related disability resulting from dynamic LV outflow obstruction in HCM, and is the primary treatment option for this subgroup of severely symptomatic drug-refractory patients. (J Am Coll Cardiol 2004;44:2044–53)

© 2004 by the American College of Cardiology Foundation

HISTORICAL CONTEXT

Historically, surgery has been the primary strategy for relieving left ventricular (LV) outflow obstruction in patients with hypertrophic cardiomyopathy (HCM) and severe limiting symptoms unresponsive to maximum medical management (1,2). A recently introduced catheter-based intervention (alcohol septal ablation) has experienced a surge in popularity among interventional cardiologists (1). In the present discussion, we wish to re-emphasize the appropriate role and visibility of surgical septal myectomy in the treatment of obstructive HCM, and in the process prudently balance the presently skewed ongoing debate between percutaneous techniques and cardiac surgery.

Since the first modern reports in the late 1950s (3,4), HCM has been regarded as a genetic heart disease characterized by asymmetric LV hypertrophy and dynamic outflow obstruction (1,2,5–18). Indeed, the common nonobstructive form of HCM was not fully appreciated until the advent of echocardiography in the early 1970s (1). Despite periodic controversy (19–21), substantial clinical importance has been attributed to LV outflow obstruction through the years, with patient management often predicated on the presence (or absence) of a subaortic gradient (1,2,7–11).

However, only recently was the long-term pathophysiologic significance of obstruction leading to progressive heart failure and cardiovascular death substantiated in a large and prospectively enrolled HCM population (22). It is now generally accepted that outflow tract gradients (and associated mitral regurgitation) represent adverse consequences of HCM, cause mechanical impedance to LV ejection, and are a major cause of disabling symptoms at any age.

Surgical intervention for obstructive HCM was first performed by Cleland (23) in the United Kingdom, but the procedure was abandoned owing to high operative mortality. Subsequently, surgical techniques were pioneered in North America by Morrow (24) at the National Institutes of Health, Kirklin (25) at Mayo Clinic, and Bigelow et al. (26) at Toronto General Hospital, and then quickly adopted by other U.S. and Western European centers. Paradoxically, early surgical efforts in the 1960s went forward even though the mechanism by which obstruction occurs, that is, systolic anterior motion of the mitral valve with prolonged mid-
systolic septal apposition, had not yet been recognized, and subaortic gradients were regarded as the consequence of a sphincter-like, muscular outflow tract contraction ring (5,6,24).

THE SURGICAL APPROACH

Surgery for obstructive HCM, traditionally performed in specialized tertiary centers, has evolved over the past four decades, from ventricular septal myotomy (i.e., without muscular resection) (26), to the classic Morrow myectomy (24). More recently, an extended and more extensive myectomy (up to about 7 cm long compared with 3 cm for the standard Morrow resection), combined with repair of mitral valve and subvalvular abnormalities, is practiced by some surgeons (27–30).

Septal myectomy is performed through an aortotomy. A rectangular trough is created by first making two parallel longitudinal incisions in the basal septum. Incisions are extended distally and then transversely connected proximally below the aortic valve and distally just beyond the level of mitral–septal contact and subaortic obstruction (with standard Morrow myectomy) or to mid-ventricular level at the base of papillary muscles (with extended myectomy), yielding 3 to 12 grams of septal muscle. It has been prudent practice to perform myectomy under intraoperative transesophageal echocardiographic guidance to directly monitor the efficacy of the resection (to identify the level of obstruction and distribution of septal hypertrophy) and allow for possible surgical revision.

Mitral valve repair, in addition to myectomy, may be most appropriate for selected patients with severe mitral regurgitation caused by primary valvular disease (e.g., myxomatous or rheumatic or ruptured chordae) (31–34). Occasionally, if intrinsic mitral valve disease is of sufficient severity to preclude repair, or the proximal septum is only mildly thickened and the risks for either septal perforation (by excessive muscular resection) or residual post-operative obstruction (by inadequate resection) are increased, then replacement with a low-profile mitral prosthesis without myocardial preservation techniques and post-operative care (31,35,36). Mitral valve replacement is, however, not routinely recommended as a primary treatment for obstruction, because of the potential post-operative complications related to durability, thromboembolism, and anticoagulation (1,2,37).

Occasionally, greatly elongated and flexible mitral leaflets will contribute substantially to the generation of mitral–septal contact (38,39). In such selected cases, mitral valve plication combined with myectomy has been performed to restrict mitral valve motion and allow for more complete relief of subaortic obstruction and mitral regurgitation (32,33,39–42). Septal myectomy also offers an opportunity to repair associated major cardiac lesions such as atherosclerotic obstructive coronary artery disease or forms of fixed aortic stenosis, or surgically treat atrial fibrillation with the MAZE procedure (43,44).

TRADITIONAL ROLE FOR SEPTAL MYECTOMY

Limiting exertional dyspnea (often with anginal or atypical chest pain), fatigue, and occasionally orthopnea, paroxysmal nocturnal dyspnea, or syncope can frequently be controlled largely by conventional drug treatment with negative inotropic agents such as beta-blockers, verapamil, and disopyramide (1,2,7,9–11) (Fig. 1). However, septal myectomy is the preferred treatment intervention should such heart failure symptoms become refractory to maximal medical management with substantial lifestyle limitation equivalent to New York Heart Association functional classes III or IV, in the presence of LV outflow tract obstruction (gradient ≥50 mm Hg under resting [basal] conditions or when physiologically provoked with exercise) (1,2) (Fig. 1). Children with obstruction may be regarded as surgical candidates when experiencing somewhat lesser degrees of limitation.

Intervention with septal myectomy (or alcohol ablation) based primarily on other disease features such as atrial fibrillation or unexplained syncope, in patients with the nonobstructive form of HCM, or in asymptomatic (or mildly symptomatic) patients with outflow obstruction, is not recommended. Of particular note, these guidelines governing the selection of HCM patients for myectomy represent the contemporary recommendations of the 2003 American College of Cardiology–European Society of Cardiology Expert Consensus Panel on the Management of HCM (1). Furthermore, it should be emphasized that the stated guidelines governing selection of patients for surgical septal myectomy are identical to those for alcohol septal ablation (1).

SURGICAL RISKS

The evolution of septal myectomy, aided by improved myocardial preservation techniques and post-operative care, as well as intraoperative echocardiography, has produced substantial reduction in operative mortality. In the 1980s, reasonably high operative mortality rates of ≥5% were reported from some centers, disproportionately reflecting the initial surgical experience of up to 40 years ago (23,24,45–49). However, over the last 10 to 15 years, myectomy has been performed with low mortality rates of 1% to 2% or even less (although somewhat higher with associated coronary artery bypass grafting or valve replacement) (46,49–52). Of particular note, the major centers performing septal myectomy report virtually no operative deaths in the most recent consecutive cases (including children) spanning the last decade (e.g., involving up to >250 cases per institution) (1,52–57). It is most appropriate
to cite these very low contemporary mortality rates to current candidates for myectomy, rather than to characterize the risks of surgery with older and obsolete data. Such surgical considerations are predicated on the strong preference that septal myectomy be performed at centers (and by surgeons) having considerable experience with obstructive HCM, and in which patient outcomes have been analyzed.

**POST-SURGICAL RESULTS**

**Heart failure symptoms.** Based on the experience and data assembled from more than 25 centers worldwide over almost 45 years (1,2,9,10,27–33,35,39–42,45–73), septal myectomy is established as a proven approach for reversing the consequences of heart failure by providing permanent amelioration of obstruction (and relief of mitral regurgitation) at rest, and restoring functional capacity and an acceptable quality of life at any age, exceeding that achievable with chronic administration of cardioactive drugs (1). These salutary benefits are demonstrable subjectively by patient history and objectively by increased treadmill time, maximum workload, peak oxygen consumption, and improved myocardial oxygen demand, metabolism, and coronary flow (66–69).

Gradient reduction results from basal septal thinning with resultant widening of the LV outflow tract area (and re-direction of forward flow with loss of the drag and Venturi effects on mitral valve) (15–17), and consequently abolition of systolic anterior motion of the mitral valve and mitral-septal contact (16,18,65,70,71,73). Mitral regurgitation is usually virtually eliminated without the need for additional mitral valve surgery (72), left atrial size (and possibly the long-term risk for atrial fibrillation) are reduced (7,11,28,74), and LV systolic and end-diastolic pressures as well as wall stress are normalized (1,2,7,11,15,72,73,75). **Long-term survival.** Whether relief of outflow obstruction by septal myectomy also extends the longevity of patients with HCM has been an important but largely unresolved issue, owing to the impracticality and ethical considerations involved in designing a controlled trial comparing patients randomized to surgery and other treatments. Nevertheless, previous reports (46,49,52–55,59–61,64) and a recently available retrospective and controlled analysis of the Mayo Clinic surgical series (75) provide evidence that myectomy results in excellent long-term survival, may alter the natural history of the disease, and consequently obstructive HCM could be regarded as a surgically correctable form of heart failure in many severely symptomatic patients. After septal myectomy, long-term actuarial survival was 99%, 98%, and 95%, at 1, 5, and 10 years, respectively (when considering HCM-related mortality). Survival of myectomy patients did not differ from that expected in a matched general U.S. population and, in fact, was superior to that achieved by non-operated obstructed patients (75). Myectomy was also associated with reduced long-term risk for sudden cardiac death (75), suggesting that the long-term consequences of surgical myectomy and ablation may well be paradoxical in this regard—that is, myectomy can decrease sudden death risk, whereas ablation may increase that risk (at least in some patients) (1). However, relevant long-term data for alcohol septal ablation will not be available for decades.

Figure 1. Presentation and treatment strategies for patient subgroups within the broad clinical spectrum of hypertrophic cardiomyopathy (HCM). AF = atrial fibrillation; DDD = dual-chamber; ICD = implantable cardioverter-defibrillator; MAZE = surgical procedure to abolish atrial fibrillation; PV = pulmonary vein; SD = sudden death; w/o = without. *No specific treatment or intervention indicated, except under exceptional circumstances. Adapted from Maron et al. (1) and reproduced with permission of the American College of Cardiology.
The impetus to developing alternative strategies for relieving LV outflow obstruction in severely symptomatic HCM patients is based on the awareness that not all patients desiring of surgery can be regarded as satisfactory candidates (1,2) (Fig. 1). For example, there may be important geographic issues (and resistance to travel) for some patients without ready access to a specialized center within the U.S. and particularly in countries without an experienced surgical option, as well as medical conditions constituting obstacles to low-risk surgery—for instance, co-morbidity or particularly advanced age, or insufficient patient motivation (1).

Pacing. In the early 1990s, dual-chamber pacing was offered as an alternative to surgery to reduce outflow obstruction and heart failure symptoms (76–79). Observational studies attributed considerable benefit to pacing, but subsequent data from randomized trials demonstrated gradient reduction to be modest and inconsistent, and the perceived functional improvement largely explained as a placebo effect (69,77–79). Although a small subset of mostly older patients may benefit from implantation of a dual-chamber pacemaker, this treatment has fallen from favor as a primary alternative to myectomy in obstructive HCM and has evolved to only a limited role (1).

Alcohol septal ablation. A nonsurgical, catheter-based technique (known by a number of acronyms) has recently emerged as an additional interventional therapy for obstructive HCM—in the process generating considerable visibility at the expense of the older surgical option (80–90). Alcohol septal ablation is a percutaneous approach in which 1 to 3 m1 of 96% to 98% alcohol is introduced into a major septal perforator artery to create necrosis and permanent myocardial infarction in the proximal septum (80–90). Subsequent intramyocardial septal scarring (91) leads to progressive LV thinning, restricted septal excursion, outflow tract enlargement, and consequent reduction in obstruction and mitral regurgitation, thereby mimicking the remodeling that results from myectomy. Therefore, alcohol ablation is a unique therapeutic strategy, in which hemodynamic and clinical benefit is promoted by virtue of intentionally creating myocardial damage.

THE CHALLENGE OF ALCOHOL SEPTAL ABLATION TO SURGERY

We are concerned that the unbridled enthusiasm in interventional practice for alcohol septal ablation (88,90–94) has become excessive without proper technical regulation and training requirements. This circumstance has also apparently obscured the appropriate selection of patients for major intervention, and has far too often made this new percutaneous strategy the initial treatment for symptomatic patients with obstructive HCM, and in the process distorted the management strategies for patients within this heterogeneous disease spectrum. Unfortunately, in increasing numbers, the surgical option is being relegated to those patients referred directly to surgeons or with failed ablations (a clinical scenario in which surgical myectomy is more difficult) (95), or portrayed in a negative light with the potential risks exaggerated while those attributable to ablation are minimized (96). Remarkably, a recent editorial (96) misrepresented management strategies in HCM by completely excluding surgery from the overall HCM treatment algorithm, thereby arbitrarily declaring myectomy to be outdated and obsolete. These developments could unnecessarily undermine future patient access to what should be considered the preferred treatment for symptomatic obstructive HCM (i.e., septal myectomy).

Of note, even though the acknowledged hemodynamic and symptomatic criteria for the selection of patients undergoing either myectomy or ablation are the same (1), the vast number of alcohol ablations performed over the last four to six years (estimated >3,500 worldwide) has reached epidemic proportions, far exceeding—by 10- to 35-fold—the number of surgical myectomies during the same time period and also the total number of operations performed worldwide over 45 years (88). Paradoxically, HCM surgery in Germany is now in danger of extinction because of the euphoria for alcohol ablation, despite the fact that myectomy was pioneered in Europe 40 years ago by German surgeons (45); however, this is not the case in many other European countries (such as France and Sweden) where alcohol ablations have been performed in only limited numbers.

To account for the excess number of alcohol septal ablations performed over a short period of time, it is undeniable that the threshold for limiting symptoms and outflow gradient has been lowered well below that generally recommended for myectomy (1,92–94). Furthermore, it has been the practice at some centers to target patients for alcohol septal ablation by provoking outflow obstruction with non-physiologic methods, for example, administration of dobutamine, a powerful inotropic drug known to induce subaortic gradients even in normal hearts (84,87,88,97–99), and the use of which has been strongly discouraged (1). These less strict patient selection criteria for alcohol ablation contrast sharply with the contemporary international guidelines of the 2003 American College of Cardiology–European Society of Cardiology consensus panel (1).

Obstacles to surgical myectomy derive from certain emerging patterns, such as the difficulties perceived by many cardiologists acting as “gate-keepers” for referring patients with obstructive HCM to surgery (particularly if alternative centers are required) (73). Certainly, economic pressures in the cardiology marketplace may understandably skew treatment choices toward catheter–based interventions, which can be performed promptly in the laboratory. Surgical septal myectomy has been traditionally performed in tertiary referral centers with subspecialists who are knowledgeable about the HCM disease process. Similarly, it is preferred that alcohol ablation be undertaken in centers having a
comprehensive understanding of HCM and surgical myectomy, rather than preferentially in interventional practices focused solely on ablation, to allow for prudent management decisions in an environment not unduly biased toward either therapeutic option. Certainly, the perceived relative simplicity of alcohol ablation has resulted in less experienced practices performing this technique without the advantage of formal training, or an expansive cardiac assessment which is necessary for a heterogeneous and complex disease such as HCM.

THE CASE FOR SURGERY: THE “GOLD STANDARD”

Although surgery and alcohol septal ablation both reduce LV outflow obstruction and symptoms, these two interventional options cannot be regarded as entirely equivalent procedures. For example, two single-institution comparison studies report certain end points (gradient reduction and peak oxygen consumption with exercise) to be superior with surgical myectomy (66,85). Indeed, with a well-performed myectomy, patients can expect a preoperative gradient of any magnitude at rest to be invariably reduced to 0 to 10 mm Hg and not recur over time (1), and to be much less variable than reported short-term after alcohol ablation. Because available follow-up information is considerable for surgery over an eight-fold greater period of time (i.e., 45 years) than for ablation (about 5 years with average cohort follow-up <2 years) (88), it remains unresolved as to whether ablation-related benefits will prove to be sustainable and truly long-lasting as with surgery. Also, immediate relief of marked outflow obstruction, which may be necessary in some particularly symptomatic patients, can only be achieved with surgical intervention, because alcohol ablation requires gradual and unpredictable remodeling with progressive scarring for up to one year in order to effect consistent gradient reduction (1,81).

Finally, rates of permanent pacemaker implantation for procedure-related complete heart block are 10-fold higher in patients undergoing ablation (5% to 25% of patients, many who are young) (1,87,88,100,101), and some patients are now receiving implantable defibrillators for high-risk status created by the ablation itself (102). Therefore, based on current practice and results, the most complete, permanent, and pure repair for severely symptomatic patients with obstructive HCM and heart failure can be expected with surgical myectomy.

It should be emphasized that intramyocardial scarring of the septum is not a consequence of septal myectomy (although localized endocardial thickening can occur) (103), nor is there evidence that surgery increases the risk for ventricular fibrillation and sudden death (1,2,73,75) or predisposes to LV systolic dysfunction (104). However, there are important unresolved issues surrounding the long-term clinical significance of the potentially arrhythmogenic substrate created by alcohol-induced myocardial infarcts (either transmural or multi-focal) (91,102). Given that many patients with HCM already harbor a pre-existing and unpredictable predisposition to ventricular tachyarrhythmias (1,2,105–109), it is likely that this additional necrosis and scarring could only enhance the level of electrical instability and thereby constitute a risk factor for life-threatening arrhythmias and sudden death in susceptible patients (9,107). This circumstance was documented by the recent report of potentially lethal arrhythmic events frequently occurring shortly after ablation (102). These considerations apply, in particular, to youthful patients with long and unpredictable periods of future risk (1,2,105–109) in whom the “trade-off” with reduced obstruction derived from alcohol ablation may not convey a net benefit. However, to date, there has been little apparent reluctance to performing ablations in young patients. Certainly, although longer follow-up is needed, there is sufficient reason to presume (based on experience with atherosclerotic coronary artery disease) that even the relatively small infarcts produced in HCM patients by alcohol ablation could well increase subsequent risk for an arrhythmic event or death (110).

Because sudden death due to ventricular arrhythmia may occur unexpectedly decades after diagnosis (1,2,105–109), the relatively short follow-up available after septal ablation at this time precludes knowledge regarding the magnitude of that risk. Therefore, these remaining uncertainties can only be resolved by comprehensive post-ablation follow-up studies over many years. Unfortunately, however, there are as yet virtually no systematic reports characterizing arrhythmias or assessing risk stratification after ablation. Surgical myectomy and alcohol ablation have not been subjected to a randomized trial, but such a study design seems unlikely given the numerous ethical and practical obstacles, including the substantial and largely consistent observational data already available for each technique, and the anticipated obstacles to organizing such an investigation of sufficient duration to assess late occurring cardiac events.

SELECTION OF PATIENTS FOR INTERVENTION

Given the aforementioned considerations, specialized HCM centers which offer both septal myectomy and ablation consistently express a strong preference for surgery, especially in younger patients (<55 years), but always in the presence of severe drug-refractory heart failure symptoms (New York Heart Association functional classes III/IV) (Fig. 2). Although there are few absolute exclusions for myectomy, alcohol ablation would be most appropriately reserved largely for specific patient subgroups including those of advanced age, with significant co-mortality and relative contraindications to surgery, or with a strong personal preference for avoiding an operative procedure—in whom proximal ventricular septal anatomy and septal perforator distribution and size are also judged appropriate (1,88,111) (Fig. 2). Alcohol ablation should be, however, strongly discouraged in children or young adults, because of
Septal Myectomy  
- Age < 55 years (and children)  
- Obstruction due at least in part to anomalies of subaortic apparatus  
- Intrinsic mitral valve disease (severe mitral regurgitation)  
- Acute gradient reduction required  
- Presence of coexisting diseases: coronary artery disease, fixed aortic stenosis, atrial fibrillation (or MAZE)  
- Particularly high gradients and extreme LVH  
- Coronary anatomy not amenable to ablation  
- Previous alcohol ablation unsuccessful

Alcohol Septal Ablation  
- Age ≥ 55 years  
- Unfavorable surgical candidate with significant co-morbidity  
- Patient unwillingness to undergo surgery  
- No access to surgical center

Dual Chamber Pacing  
- Not candidate for either myectomy or alcohol ablation

Figure 2. Each of the individual factors which favor management decisions for respective therapeutic options in patients with obstructive hypertrophic cardiomyopathy and drug-refractory severe symptoms (New York Heart Association functional classes III/IV). LVH = left ventricular hypertrophy; MAZE = surgical procedure to abolish atrial fibrillation.

The future management of obstructive HCM will require expanded patient access to surgery, to be promoted in selected regional centers for which at least 10 myectomy operations would be performed annually. This would, in a proactive fashion, counteract the possible contraction of surgical services available to patients in the future. At
present, with the permanent closure of both the medical and surgical HCM programs at the National Institutes of Health (Bethesda, Maryland), a limited number of North American centers remain most dedicated to the HCM surgical option: Mayo Clinic, Cleveland Clinic, and Toronto General Hospital, and emerging programs at St. Luke’s-Roosevelt Hospital Center (New York) and Tufts-New England Medical Center (Boston).

CONCLUSIONS
At this crossroads in the management of obstructive HCM, it would seem prudent to adopt a measure of restraint before allowing an intoxication with novel interventional technology—relatively untested over time (alcohol ablation)—to impair the availability of the established treatment (septal myectomy) which has served patients with HCM exceedingly well over decades and continues to merit the confidence of the cardiovascular community. However, our arguments for surgery are not intended to represent an indictment or rejection of the alcohol septal ablation procedure. To the contrary, alcohol ablation is a promising alternative therapy for selected patients and an important addition to the therapeutic armamentarium of obstructive HCM. However, its ultimate role in management is not yet fully defined or resolved, and requires further long-term evaluation. Indeed, there is presently no justification for promoting alcohol ablation as the standard primary therapeutic strategy for all severely symptomatic patients refractory to maximal medical management and with marked obstruction to LV outflow. Septal myectomy remains the gold standard treatment option for this HCM patient subset.

Reprint requests and correspondence: Dr. Barry J. Maron, The Hypertrophic Cardiomyopathy Center, Minneapolis Heart Institute Foundation, 920 E. 28th Street, Suite 60, Minneapolis, Minnesota 55407. E-mail: hcm.maron@mhif.org.

REFERENCES
20. Reprint requests and correspondence: Dr. Barry J. Maron, The Hypertrophic Cardiomyopathy Center, Minneapolis Heart Institute Foundation, 920 E. 28th Street, Suite 60, Minneapolis, Minnesota 55407. E-mail: hcm.maron@mhif.org.
30. Minakata K, Dearani JA, Nishimura RA, et al. Extended septal myectomy for hypertrophic obstructive cardiomyopathy with anom-


71. Franke A, Schöndube FA, Kühl HP, et al. Quantitative assessment of the operative results after extended myectomy and surgical resection of the subvalvular mitral apparatus in hypertrophic obstructive...


