Controversies Revisited

Surgical Septal Myectomy Versus Alcohol Septal Ablation
Assessing the Status of the Controversy in 2014

Barry J. Maron, MD; Rick A. Nishimura, MD

In hypertrophic cardiomyopathy (HCM), left ventricular (LV) outflow tract obstruction, caused by mitral valve systolic anterior motion (SAM) with elevated intracavitary LV pressures, can produce disabling symptoms of heart failure and excess cardiovascular mortality.1-7 Outflow gradients are common in HCM, present in 70% of patients at rest or with physiological exercise6 (Figure 1). Fifty years ago, early HCM investigators recognized the importance of obliterating LV outflow obstruction (and mitral regurgitation) and restoring normal hemodynamics, initially with the septal myectomy operation advanced by Dr Andrew Morrow at the National Institutes of Health.6,7 However, HCM has not been immune to controversy, and through the years, several debates have focused on the significance of dynamic outflow obstruction and its treatment.7 The most recent of these conversations concerns the most effective strategy for reducing gradient and symptoms, triggered by the introduction of catheter-based percutaneous alcohol septal ablation (ASA) as an alternative to myectomy8-10.

The nonsurgical technique, introduced by Professor Ulrich Sigwart at the Royal Brompton Hospital in 1994,8 involves injection of 1 to 4 mL of 96% ethanol into the first septal perforator branch of the left anterior descending coronary artery to produce a basal septal myocardial infarction and ultimately remodeling of the LV outflow tract. ASA avoids the recovery time with loss of work, residual discomfort, and anxiety associated with surgery. It was soon enthusiastically embraced and heavily promoted by many clinicians and interventional cardiologists, initially in Europe, thereby expanding the treatment armamentarium of HCM and triggering a polarized and some interventionalists have suggested? Has the myectomy operation become obsolete in an era dominated by interventional techniques? Or does surgery remain the standard for most patients, with ASA only a selective alternative, as suggested by most HCM experts and the available consensus guidelines? We believe the fundamental issue is more nuanced, importantly concerning proper patient selection and preference, and the matching of the most appropriate septal reduction therapy to the individual HCM patient.

History of Alternatives to Myectomy
Surgical myectomy has been considered the gold standard for the treatment of severe, medically refractory symptoms resulting from LV outflow tract obstruction2,3,20-25 (Figure 1). Excellent acute hemodynamic results and sustained clinical improvement have been documented over long-term follow-up.1-3,20-25 However, the myectomy operation requires extensive surgical expertise, which may not be readily available in all centers or practices caring for patients with HCM.24 In addition, older patients and those with important comorbidities may be at increased risk during open heart surgery. Therefore, identifying effective alternatives to myectomy for selected patients has been an objective within comprehensive HCM management for >25 years.2,20,23 Indeed, in the early 1990s, a time when myectomy was associated with relatively high mortality (up to 8%), dual-chamber pacing with short A-V delay was promoted as a surgical alternative for gradient and symptom relief.26 After an initial period of enthusiasm, pacing was largely abandoned as evidence eventually became available from randomized, double-blind, crossover studies that symptom improvement reported by patients was essentially a placebo response.26 Some functional benefit was evident in the elderly and those with underlying conduction system disease.

Interest in pacing was soon replaced by interest in the rapidly evolving ASA. The striking increase in the number of ASA procedures was initially driven by an unbridled enthusiasm, a “bandwagon” effect, and publication bias in which new treatment innovations inevitably dominate the literature.
initially, as well as a natural preference for less invasive approaches. Ultimately, the number of ASA procedures grew to far outnumber the myectomy operations performed overall in any given year. It has been estimated that the total number of ASAs in the last 10 years exceeds by a large margin all myectomy operations performed in almost 50 years, with the impetus from the interventional cardiology community. In dedicated HCM centers, however, surgery clearly predominates, with a myectomy-to-ablation ratio in the range of 5:1 to 20:1.

This heightened interest in ASA led to the virtual abandonment of myectomy throughout Europe, although there is some recent evidence of a surgical revival in Italy, the Netherlands, and the United Kingdom. Paradoxically, the interest in LV outflow obstruction created by ASA has also stimulated a sharp rise in referrals for myectomy in US centers.

Guidelines

The emergence of ASA and the controversy it has triggered were responsible in part for an ACC/European Society of Cardiology consensus document and ACC/AHA guidelines, 10 years apart, agreed explicitly on 2 basic principles (Figure 1): (1) Surgical myectomy is the preferred (gold standard) and safest septal reduction procedure for most severely symptomatic obstructive HCM patients refractory to maximum medical management, and (2) ASA is not regarded as the primary treatment option for such patients with a similar severity of functional limitation but rather as a useful, selective alternative to septal myectomy for patients of advanced age, patients at high operative risk as a result of important comorbidities, or those with a strong personal preference to avoid surgery. ASA can be performed only when the coronary artery anatomy is suitable and cannot be undertaken when there is a need for concomitant cardiac surgery (eg, coronary artery disease requiring bypass grafting; resection of a subaortic membrane; intrinsic mitral valve disease dictating repair or replacement).

Because the 2011 ACC/AHA management guidelines resolved in large measure the debate of myectomy versus ASA, we see no reason to dispute those unbiased and prudently constructed recommendations here. However, the degree to which the guidelines have actually influenced practice patterns is uncertain, and a mismatch between the 2 may currently persist. A major factor contributing to the high volume of ASA procedures is the limited number of centers with sufficient surgical expertise for properly performing septal myectomy.

<table>
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<tr>
<th>Advantages</th>
<th>Disadvantages</th>
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<tr>
<td>Symptom relief and improved quality of life known to persist long term</td>
<td>Open heart surgery; requires thoracotomy/cardiopulmonary bypass, 5-d hospitalization, and recovery period of several weeks</td>
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<tr>
<td>Relief of outflow gradient is immediate and sustained; reoperation rarely necessary</td>
<td>Requires a cardiac surgeon experienced specifically with myectomy (may necessitate patient referral/travel)</td>
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<td>Alters disease course long term by affording extended survival equivalent to that of the general population</td>
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<td>Permits direct visualization of complex outflow tract anatomy by the operating surgeon</td>
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<td>Allows identification of mitral apparatus abnormalities; resection can be tailored precisely to the distribution of septal thickening</td>
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<td>Permits repair of associated cardiac lesions, if necessary</td>
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<td>Rarely requires permanent postoperative device therapy</td>
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<tr>
<td>No postoperative intramyocardial scar</td>
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<td>Can be performed appropriately in children and young adults; better efficacy in patients &lt;65 y of age</td>
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Table 1. Advantages and Disadvantages of Surgical Myectomy

Figure 1. Treatment algorithm for hypertrophic cardiomyopathy (HCM) patients with heart failure symptoms of exertional dyspnea with or without chest pain. LVOT indicates left ventricular outflow tract; and NYHA, New York Heart Association.
interventional cardiologists available and willing to perform ASA. Intuitively, most patients would prefer the less invasive septal reduction approach, if indeed the expected outcomes from myectomy and ASA were the same. It is therefore important to continue interrogating the evolving evidence on the relative risks and benefits of the 2 procedures to determine the optimal strategy for individual HCM patients (Tables 1 and 2).

Comparison of Septal Reduction Treatments

In principle, the clinical indications for myectomy and ASA are the same: marked LV outflow obstruction usually caused by SAM (≥50-mmHg gradient at rest or with physiological exercise) that is responsible for progressive heart failure symptoms and functional limitation that significantly affects quality of life (in adults, equivalent to New York Heart Association functional classes III/IV, or earlier with less severe limitation in selected children and adult patients) in patients refractory to a variety of largely negative inotropic drugs1-3,20-28 (Figures 1 and 2). However, in reducing gradients, myectomy and ASA differ in several important respects, which taken together support the guideline position that surgical myectomy is the preferred treatment option for most such HCM patients.

LV Outflow Tract Anatomy

The heterogeneous and complex LV outflow tract morphology characteristic of HCM is most amenable to the myectomy operation in which the surgeon has the advantage of direct anatomic visualization.1,3,20,23,27,28 This approach permits overall reconstruction of the outflow tract, taking into account abnormalities such as muscular midcavity obstruction resulting from anomalous anterolateral papillary muscle insertion directly into mitral valve, aberrant intraventricular muscle bundles, displaced papillary muscles, and mitral leaflet elongation, all of which may contribute to the outflow gradient.1,3,20,23,27 Given these considerations, the extended myectomy modification of the classic Morrow procedure has been developed to more effectively abolish obstruction and to normalize LV pressure.22,23,27

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Table 2. Advantages and Disadvantages of Alcohol Septal Ablation

<table>
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<tr>
<th>Advantages</th>
<th>Disadvantages</th>
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<tr>
<td>Percutaneous technique (does not require thoracotomy, cardiopulmonary bypass)</td>
<td>Procedural mortality not negligible</td>
</tr>
<tr>
<td>Short in-hospital stay and rapid recovery</td>
<td>Produces potentially large, transmural infarct with arrhythmogenic potential that could increase arrhythmia/sudden death risk in susceptible patients; may require prophylactic implantable defibrillator</td>
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<tr>
<td>Avoids identifying an expert myectomy surgeon who may not be readily available geographically</td>
<td>Procedure confined to inflexible anatomic distribution of septal perforator artery; cannot be easily tailored to complex left ventricular outflow tract anatomy in some patients</td>
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<tr>
<td>May be a more appropriate option than surgery for many elderly patients and those with comorbidities</td>
<td>Not infrequently causes heart block requiring permanent pacemaker</td>
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<td>Evidence for efficacy in older patients &gt;65 y of age</td>
<td>Relief of gradient is not immediate, requiring several weeks to fully evolve</td>
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<td></td>
<td>Ineffective in patients with highest gradients or extreme septal thickness and often requires repeat interventions</td>
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<td></td>
<td>Should not be performed in children and young adults</td>
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Figure 2. Significance of left ventricular (LV) outflow obstruction in patients with hypertrophic cardiomyopathy (HCM; A) and the benefit of interventions to relieve gradients and symptoms (B and C). A, Greater risk for HCM-related progressive heart failure or heart failure or stroke death is associated with outflow gradients ≥30 mm Hg at rest. NYHA indicates New York Heart Association; and RR, relative risk. Reproduced from Maron et al5 with permission from the publisher. Copyright © 2003 Massachusetts Medical Society. B, Abolition of LV outflow gradient by surgical septal myectomy is associated with enhanced quality of life and extended long-term survival (with respect to all-cause mortality), similar to that expected in the age- and sex-matched general US population, and exceeding that in a comparison group of symptomatic nonoperated patients with outflow obstruction. Reproduced with permission from Ommen et al. Long-term effects of surgical septal myectomy on survival in patients with obstructive hypertrophic cardiomyopathy. J Am Coll Cardiol. 2005;46:470–476.25 Copyright © 2006 Elsevier BV. C, Freedom from death and severe symptoms after surgical myectomy and alcohol ablation, specifically with interventions, in individuals ≤65 years of age. Reproduced from Sorajja et al.10
An additional potential advantage of the surgical myectomy approach is the opportunity to repair mitral valve abnormalities. Indeed, greatly elongated mitral leaflets are not an uncommon component of obstructive HCM morphology, and there may be concern that, despite an adequate myectomy, the enlarged mitral valve may create septal contact. Differences of opinion are evident among operating surgeons about the potential importance of the mitral valve in residual LV outflow tract obstruction. Some myectomy surgeons have advocated selective mitral valve plication (or anterior leaflet extension) combined with myectomy as necessary to ensure effective and optimal relief of LV outflow tract obstruction. Other successful myectomy surgeons have found little or no reason to consistently repair the mitral valve. The decision of whether to repair the elongated mitral valve at the time of myectomy is a judgment made by the operating surgeon in consultation with the managing cardiologist. Mitral valve replacement is an exceedingly uncommon practice for experienced myectomy surgeons. Combining myectomy with mitral valve replacement is not a standard operation.

In contrast, ASA is a “blind” approach without the advantage of direct anatomic visualization and is restricted by the size and distribution of the septal perforator artery and its fixed anatomic relationship to the target site of SAM–septal contact. In addition, ASA is ineffective in patients with substantial LV hypertrophy (>25-mm wall thickness), since sufficient septal thinning cannot be reliably achieved.

LV Outflow Gradient

Both ASA and myectomy are effective in relieving mechanical impedance to LV outflow. Whereas any intervention that relieves outflow gradient (and normalizes LV pressures) will improve symptoms and reverse the progression of heart failure in properly selected HCM patients, myectomy produces more complete gradient relief, particularly in patients <65 years of age.

Gradient reduction with ASA is generally most favorable in older patients >65 years of age who have lesser degrees of LV hypertrophy, consistent with the guidelines that favor ASA as a potential surgical alternative largely in patients of advanced ages. Residual gradients are more frequent and higher after ASA than with myectomy, often because the area of SAM–septal contact cannot be reached optimally by the distribution of the targeted septal perforator artery. Post-ASA incomplete gradient relief requires repeat intervention in ≈12% of patients and has been associated with an increase in all-cause mortality, whereas reoperation is extraordinarily rare with myectomy.

Myocardium

ASA targets the basal anterior septum with a transmural scar that may be sizable in quantitative terms, comprising ≈10% of LV mass (30% of the septum) (Figure 3). Consequently, ASA constitutes a unique therapeutic approach in which heart muscle is intentionally destroyed to achieve hemodynamic benefit, in the process contradicting a major tenet of preventive cardiology to minimize myocardial infarction/scarring. In contrast, surgical myectomy does not produce an intramyocardial scar; some endocardial fibrosis, which is neither a scar nor arrhythmogenic, may be evident at the site of muscular resection. The presence versus absence of intramyocardial scarring is a major distinction between the 2 septal reduction interventions.

The precise degree to which the alcohol-induced infarct represents an arrhythmogenic burden in a population of post-ASA patients has been the source of considerable controversy and remains incompletely resolved. Nevertheless, concern persists regarding the potentially lethal arrhythmogenic events occurring after ASA. This risk of ASA exceeds that occurring after myectomy and is probably more likely in susceptible patients with preexisting HCM-related sudden death risk markers.

In follow-up studies and some case reports, ventricular tachyarrhythmias and sudden death events have been linked to the myocardial infarct produced by ASA, and the North American Multicenter ASA Registry reports a postprocedural mortality of 26% after 9 years. Using lesser amounts of alcohol may produce smaller areas of necrosis and reduce the arrhythmogenic potential of ASA, although probably at the expense of decreased hemodynamic benefit. In practice, some clinicians have implanted cardioverter-defibrillators for primary prevention after ASA, but no predictive risk stratification model has been proposed for this specific clinical situation.
Longer-term and more complete follow-up data in the ASA population are required to resolve this question of postprocedural risk more definitively. The aforementioned considerations have stimulated preliminary initiatives to identify percutaneous alternatives to ASA, such as percutaneous plication, that are not destructive to LV myocardium and directly target the mechanism of obstruction (ie, SAM). In contrast, long-term follow-up studies after myectomy do not show an excess arrhythmic burden resulting from the operation itself. Indeed, after myectomy, there is a low event rate for sudden death or appropriate implantable cardioverter-defibrillator interventions terminating ventricular tachyarrhythmias. Therefore, myectomy, although requiring open heart surgery, represents a relatively pure intervention without a residual arrhythmogenic substrate, and rarely requires implanted devices.

**Procedure-Related Morbidity and Mortality**

Some studies have reported that overall procedural mortality is largely similar between the 2 interventions, although other reports suggest a higher death/complication rate with ASA compared with the particularly low current operative mortality for isolated myectomy at the most experienced centers (ie, <1%). This observation dispels the notion from a much earlier era that surgery is a high-risk option for patients with obstructive HCM and underscores that the apparent simplicity and safety of the percutaneous approach should be placed in perspective. However, such comparisons between surgery and ablation are difficult, given the likely differences in operator expertise and patient selection. For example, ASA is performed in a multitude of individual laboratories with diverse (and sometimes limited) experience, but outcome data are reported only from the few most established centers and practices. Therefore, the true ASA-related complication rate is not known for those laboratories in which the procedure is performed infrequently. On the other hand, most myectomy surgery occurs in only a few select programs such as the Mayo Clinic, Cleveland Clinic, Tufts Medical Center (Boston, MA), Mount Sinai, St. Luke’s–Roosevelt (New York, NY), and Toronto General Hospital.

Nonfatal procedural complications are reported with either myectomy or ASA, but most attention has focused on heart block produced by the administration of alcohol because the septal perforator artery serves the conduction system. Transient heart block is common in up to 50% of patients in the first 24 hours, but permanent complete heart block conveying lifelong pacemaker dependency is reported in ≈10% to 15% and is most likely in those patients with preexisting left bundle-branch block or possibly first-degree atrioventricular block (because ASA produces right bundle-branch block). Myectomy characteristically produces left bundle-branch block, but permanent pacing is a very rare consequence of surgery. However, it should be underscored that with either procedure inexperience promotes a lower likelihood of success and an increased complication risk. The temporizing strategy of performing ASA first, and myectomy later if ASA is unsuccessful, only increases operative and arrhythmic risk and the likelihood of pacemaker implantation.

**Postprocedural Outcome**

In addition to providing substantial and timely improvement in limiting symptoms for the vast majority of patients, surgical removal of the LV outflow gradient and normalization of intracavitary LV pressures have been shown to produce a long-term survival benefit. Operated HCM patients have an all-cause mortality no different from that of the general population and lower than that for symptomatic but nonoperated patients with outflow obstruction (Figure 2).

In patients <65 years of age, isolated myectomy shows results superior to ASA, with more favorable survival and freedom from severe symptoms (New York Heart Association class III/IV), and restoration of quality of life (Figure 2); in this age group, only ≈50% of the ASA patients became completely asymptomatic. On the other hand, ASA achieves greater symptom and gradient reduction in patients >65 years, an age group with an intuitively lower sudden death risk and for whom the percutaneous alternative to myectomy is most favored in the ACC/AHA guidelines. When ASA is, in fact, successful in terms of gradient and symptom relief, the short-term outcome appears to be similar to that of myectomy.

Short-term cohort analyses from some interventional laboratories have reported no difference in all-cause mortality or sudden death risk for patients with ASA compared with those with myectomy or the general population. However, a number of variables make it difficult to reliably compare the clinical course after ASA versus myectomy in this way: including disparate lengths of follow-up since ASA is a much newer technique with shorter and relatively brief periods of observation, often incomplete outcome or baseline risk level data, as well as the unpredictable nature of the HCM substrate itself. Furthermore, in certain individual patients, surgical myectomy may be a more prudent choice on the basis of LV outflow tract or coronary arterial anatomy, variables not accounted for in comparative group data analyses when all-cause mortality is used as the end point.

**Accessibility**

The gap in accessibility between myectomy and ASA has been a major determinant in the selection of patients for either septal reduction procedure. ASA is a widely available catheter-based technique that can be performed in virtually any laboratory without the requirement for accreditation, prior experience, or specialized training; indeed, the majority of practicing interventional cardiologists can anticipate performing ASA. This contrasts sharply with the relatively few surgeons outside dedicated multidisciplinary centers with either specific myectomy experience or even the inclination to perform this particular operation. However, in situations in which expert myectomy is not readily accessible, cardiology practices or healthcare systems may be reticent to refer patients elsewhere.
may also be hesitancy on the part of some patients without sufficient means, resources, or motivation to travel to medical centers far away from home for surgery. They will likely elect a local option, which is almost always ASA. This clinical dilemma is reminiscent of the ACC/AHA guideline recommendation for those select patients considering complex mitral valve or aortic repair to be referred to designated centers of excellence with specialized surgical experience to ensure optimal results.30

HCM Centers and Shared Decision Making
Programs dedicated to HCM patients within cardiology divisions at academic tertiary referral medical centers can help to resolve the issue of patient selection bias for septal reduction procedures.3,13,34,40,41 Comprehensive programs with multidisciplinary teams have the background, knowledge, and expertise to provide the necessary information to formulate a fully informed clinical decision. Such HCM centers include within the same institution experienced operators with a high level of expertise for both surgical myectomy and catheter-based options. Patients who are at high risk for surgical myectomy, for whom ASA is the preferred option, could be treated at any institution where there are interventionalists trained to competently perform ASA. However, competency in performing ASA requires an understanding of the such expertise complexities of HCM, as well as the experience gained in performing a number of procedures in a proctored environment, as recommended in the ACC/AHA management guidelines for HCM.3 Recent experience and data suggest that at least 50 successful procedures are required to overcome the ASA learning curve.

However, the patient who is otherwise a good candidate for septal myectomy should be provided with the choice of either myectomy or ASA using a transparent shared decision-making approach.3,13,34,41 Shared decision making provides the patient with all available data on the advantages and disadvantages of the 2 strategies, with the patient then providing his or her own preferences to arrive at a final clinical decision leading to targeted management. This process can occur directly at the HCM center of excellence41 but also at a distance with consultations connecting the patient with experts in the field.3 We have found that, with this approach to the problem, there will be a subset of patients who choose to proceed with ASA, but >80% of patients eligible for either approach will choose surgical myectomy.

Can the Debate Be Resolved by Data?
Current knowledge of ASA versus myectomy is based on observational, nonrandomized cohort data and meta-analyses, with all the inherent limitations and biases of such study designs. In cardiovascular medicine, prospective, randomized trials are performed to resolve clinical dilemmas comparing 2 competing treatment modalities such as those discussed here. Controlled trials avoid bias with regard to patient selection, operator skill and expertise, and outcome reporting.

However, as already noted, there are substantial data available comparing myectomy and ASA with regard to short-term gradient and symptom reduction,1–13,9–10 and further substantiation by an expansive, complex, prospective, randomized trial is probably unnecessary. On the other hand, at least in theory, such a trial conducted over a substantial period of time could address possible differences in survival, persistence of symptom improvement, changes in systolic function, and frequency of heart failure and sudden death events.

However, Olivotto et al42 have convincingly demonstrated that an adequately powered randomized study to address these particular clinical questions in a low-event-rate disease such as HCM is an impractical (if not impossible) consideration (Figure 4). Specifically, such an investigation would, in fact, require the initial screening of >35,000 HCM patients to enroll >500 suitable study patients in each treatment arm to compare clinical outcome as a primary end point (Figure 4). Such a cohort size exceeds the total number of patients with HCM currently identified at major institutions in the world. In addition, such a study would have the insurmountable practical obstacle of requiring many years of follow-up (probably more than a decade) and necessitating substantial long-term funding in a clinical environment in which patient randomization would constitute a major ethical dilemma.

Conclusions
Treatment options for patients with HCM have expanded substantially over the last 10 years, including the introduction of ASA to reduce LV outflow gradient and heart failure symptoms as an alternative to surgical myectomy. A debate on the relative merits of these 2 strategies has been waged over this period of time, sometimes with diametrically opposed positions and alternative interpretations of the same data. A vast literature has been assembled from both the percutaneous and operative perspectives, and consensus and guideline documents have been produced by all major cardiovascular societies.
Although both septal reduction interventions reduce LV outflow obstruction and abridge heart failure progression, surgical myectomy is most consistent in achieving optimal hemodynamic and symptomatic benefit, resulting in good quality of life and increased longevity, similar to that expected in the age- and sex-matched general population, and with procedural risks similar to (or lower than) those achieved percutaneously with ASA.

ASA is more advantageous for older patients, including those with comorbidities, although overall it is associated with a risk for sudden death or ventricular tachyarrhythmias that exceeds that of surgery. Therefore, the preponderance of evidence, expert consensus, and guideline opinion continues to favor surgical septal myectomy as the preferred treatment for most drug-refractory, severely symptomatic patients with obstructive HCM. ASA is a useful alternative option for selected patients.

Disclosures

None.

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