Role of Percutaneous Septal Ablation in Hypertrophic Obstructive Cardiomyopathy

Carey D. Kimmelstiel, MD; Barry J. Maron, MD

Case Presentation: A 58-year-old diabetic man was referred for severe progressive exertional dyspnea consistent with New York Heart Association (NYHA) functional class III. Six years earlier, he underwent coronary artery bypass grafting, complicated by a sternal wound infection.

Physical examination was notable for a bifid carotid pulse and loud apical systolic ejection murmur. Echocardiography documented hyperdynamic left ventricular (LV) systolic function and asymmetric hypertrophy confined to the basal ventricular septum (measuring 20 mm in thickness) consistent with hypertrophic cardiomyopathy (HCM). Continuous wave Doppler estimated a 65 mm Hg subaortic gradient due to dynamic systolic anterior motion of the mitral valve with septal contact. Coronary angiography showed patent bypass grafts.

Medical management with β-blockers and verapamil was ineffective in controlling symptoms. Catheter-based intervention was considered for this patient to reduce outflow obstruction and symptoms.

HCM is a relatively common genetic disease with important clinical consequences, including sudden death in the young and disability due to heart failure at any age.1,2 It is estimated that progression to NYHA functional classes III/IV associated with obstruction to LV outflow occurs in about 10% of HCM patients who are limited largely by exertional dyspnea, chest pain, fatigue, and occasionally orthopnea or nocturnal dyspnea.1,2 Long-term consequences of HCM attributable to outflow obstruction have been emphasized, particularly progression of disabling symptoms and death related to heart failure.3

Therapeutic Options in Obstructive HCM
The traditional first line of therapy to improve quality of life in HCM patients with symptoms and outflow obstruction has been administration of negative inotropic agents, including β-blockers, verapamil, and disopyramide.1,2 Although symptoms can be controlled by drug treatment, a small minority of patients may become disabled and refractory to maximum medical management, and consequently eligible for major therapeutic interventions that target relief of obstruction and mitral regurgitation.1 Historically, this strategy has been confined to the “gold-standard” ventricular septal myectomy operation,1 and substantial benefit has been attributed to this procedure over the past 45 years throughout the world.1,2

However, experience with surgery has been limited to a relatively small number of centers in North America and Europe.1 Many countries with large numbers of HCM patients do not have ready access to such surgical expertise, and some patients are not optimal candidates for operation. Therefore, alternative therapeutic options for surgical candidates with HCM have justifiably been pursued.1,3

There has been considerable interest over the past few years in a percutaneous method for relieving obstruction and symptoms that has been referred to in the literature by several names and acronyms.3–9 This procedure uses conventional interventional methodology currently available for treating atherosclerotic coronary artery disease to create necrosis of the anterior basal septum by introducing absolute alcohol directly into a proximal septal perforator artery, ultimately reducing LV wall thickness, enlarging the outflow tract and reducing mechanical impedance to LV ejection. Therefore, percu-
taneous transluminal septal myocardial ablation (PTSMA) may mimic the morphological and hemodynamic effects of surgical myectomy.

**PTSMA Technique**

The presence or absence of significant epicardial coronary artery disease, particularly in the left anterior descending (LAD) coronary artery, is documented by angiography. The baseline gradient is measured by use of an end-hole pigtail catheter, assuring that the level of obstruction is subaortic. For patients in whom the outflow gradient is either absent or small under the basal conditions, the magnitude of provokable obstruction is most appropriately assessed with physiological exercise.

Of particular importance is proper selection of the target septal perforator. The optimal method is unresolved; some operators favor a pressure and fluoroscopic-guided technique in which balloon occlusion of the septal artery is followed by fluoroscopy to identify proximal septal tissue that is the target for ablation.⁴ Most other PTSMA practitioners utilize myocardial contrast echocardiography to identify the appropriate septal perforator, which involves 2-dimensional echocardiographic monitoring during introduction of 1 to 2 mL of echo or angiographic contrast through the distal lumen of a balloon dilation catheter.⁵,⁶ Contrast echocardiography enhances the effectiveness and safety of PTSMA by avoiding arteries that supply distant regions of myocardium, as well as by limiting the number of arteries intervened, the frequency of complete heart block requiring permanent pacemaker, the amount of alcohol injected (and creatine phosphokinase levels), and fluoroscopy time. After identification of the most appropriate perforator, balloon occlusion is followed by contrast injection through the coronary guide catheter as well as the distal balloon port to document complete cessation of flow between the distal septal artery and LAD.

PTSMA is performed by injection of 1 to 4 mL of 96% to 98% ethanol into the target artery in 0.5 to 1.0 mL aliquots at 1 mL/min (Figure 1). Reduced amounts of ethanol and slower infusion minimizes complications, par-

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**Figure 1.** A, Pre-ablation. Coronary angiogram showing 2 septal perforators (arrow and arrowhead) in close proximity. Myocardial contrast echocardiography demonstrated that the first septal perforator artery (arrow) was the optimal vessel for alcohol injection. B, Pre-ablation. Baseline hemodynamics showing 110 mm Hg subaortic gradient. Post-extraystolic beat (*) augmentation of gradient (to 180 mm Hg) in association with “spike and dome” (Brockenbrough) aortic waveform. Scale: 0 to 280 mm Hg. C, Post-ablation. Angiogram shows the first septal perforator (arrow) is ablated. D, Post-ablation. Marked reduction in outflow gradient to 25 mm Hg. Ao indicates aorta; PA, pulmonary artery; and LV, left ventricle.
particularly high grade atrioventricular block.2–4 In the laboratory, the goal of PTSMA is acute reduction in resting and/or provoked gradient by 50% or to <20 mm Hg. The immediate post-ablation gradient reduction is probably due to alcohol-mediated septal necrosis and stunning, a mechanism distinct from the septal thinning and ventricular remodeling that is associated with progressive gradient reduction on long-term follow-up.5–9

Clinical Results
PTSMA has not been subjected to randomized clinical trials against the septal myectomy in patients with severe symptoms and outflow obstruction. However, observational data from US and European centers over short follow-up periods are reasonably consistent, attributing a number of favorable effects to PTSMA that generally parallel that of surgery, including gradual and progressive reduction in outflow gradient over 3 to 12 months and alleviation of symptoms.4–6

In a comparative non-randomized study at 2 independent institutions, myectomy and alcohol ablation showed a similar degree of gradient reduction.5 Another comparative analysis from a single institution showed both surgery and PTSMA to substantially reduce outflow gradients, but to a greater degree with surgery.7 A third nonrandomized study showed surgery and PTSMA to afford similar benefit in reducing LV outflow gradient, both acutely and after 1 year; however, surgical myectomy out-performed PTSMA with respect to improvement in exercise capacity.8 Patients with predominant provokable obstruction may also benefit from PTSMA.9

Although reports of symptomatic benefit after PTSMA have been based largely on retrospective and uncontrolled assessments, some objective data are now available describing clinical improvement in terms of measured exercise capacity by treadmill exercise time and peak oxygen consumption. Significant and progressive enhancement in exercise treadmill time or maximum workload or peak oxygen consumption have been reported to be associated with gradient reduction in follow-up studies over 3 to 18 months.4–6,8–9

Complications
Complication rates after PTSMA have declined since the initial reports because of evolution of the “learning curve” for operators. Specifically, there is greater appreciation for identifying the most appropriate septal vessel for intervention (Figure 1 and Figure 2) and using smaller amounts of alcohol (introduced more slowly) creating more limited areas of myocardial necrosis and scarring.4–6,10 PTSMA-related mortality has been reported at up to 4%, but in experienced centers is currently 1% to 2% (similar to that of surgery).7,9 Conduction abnormalities are relatively common complications of PTSMA, with permanent right bundle branch block and transitory heart block in about 50% and high-grade atrioventricular block requiring permanent pacemakers in 5% to 20%. Particular concern regarding complete heart block relates to its occasional unheralded occurrence after PTSMA, mandating inpatient monitoring for 4 to 5 days. A profound complication is anterior myocardial infarction due to ethanol reflux from the septal perforator down the LAD, avoidable by scrupulous balloon positioning. Other rare complications include coronary dissection, perforation, and thrombosis.

Selection of Patients for PTSMA
Selection of patients for PTSMA (Figure 3) includes those with severe symptoms (ie, NYHA functional classes III or IV) refractory to maximal medical management associated with a LV outflow gradient ≥50 mm Hg at rest or after provocation (with physiologic exercise) and basal septal thickness ≥18 mm, particularly if such patients have advanced age, with important co-morbidity or contraindications, or with insufficient motivation for surgery. Selected obstructed patients in advanced functional class II may be eligible for intervention, such as when symptoms interfere with their occupation. Dobutamine, an inotropic and catecholamine-inducing drug, and powerful stimulant of subaortic gradients in normal hearts or cardiac diseases other than HCM, is not recommended to provoke LV outflow gradients to assess the appropriateness of PTSMA in HCM.1,3 PTSMA is not indicated in the nonobstructive form of HCM.

However, patients with congenital anomalies of the mitral valve apparatus, unfavorable distribution of septal hypertrophy with mild proximal thickening, associated heart lesions requiring surgical correction, or anatomically unsuitable septal perforators should not undergo PTSMA.1

Limitations and Unresolved Issues
Although PTSMA has found a place in the therapeutic armamentarium of HCM, several important considerations persist. The first issue concerns the potential long-term consequences of the intramyocardial septal scar (often transmural) intentionally produced by PTSMA (and which is not a consequence of septal myectomy).1,3 Even before PTSMA, patients may already harbor an electrically unstable myocardial substrate prone to reentrant ventricular arrhythmias. This raises the reasonable possibility that the resultant septal infarct could enhance (but certainly not reduce) likelihood of sudden death in some patients. There are, however, practical difficulties in assessing this potential complication of PTSMA, given the short follow-up period (ie, <5 years) currently available for the vast majority of patients, as well as the particularly long risk period implicit in young HCM patients. The vast numbers of patients treated with PTSMA, scattered among many small centers and practices, make it difficult to assemble precise long-term follow-up data and discern whether inevitable sudden deaths are a
It is counterintuitive to promote PTSMA as a treatment intervention to reduce risk for sudden death in HCM. Therefore, it is most prudent to discourage PTSMA in young adults (and especially children) when the surgical option is available, given the long (essentially lifetime) risk period for arrhythmia-mediated sudden death, at least until more data regarding the long-term consequences of PTSMA are available. Indeed, there is a strong preference in HCM centers experienced with both procedures to refer younger patients for septal myectomy. Randomized trials of PTSMA versus surgery are unlikely to clarify the issue of late post-procedural clinical events because of practical obstacles in designing studies of sufficient duration to encompass the substantial period of risk.

A second major area of concern is the large number of PTSMA procedures performed over a relatively short period of time, unavoidably suggesting a lower threshold in recommending this procedure than for surgery. There have been an estimated 3000 PTSMA procedures performed worldwide in just 5 years. Therefore, PTSMA has probably been performed at a rate of 10 to 30 times that of surgery during this time, and has probably already surpassed the number of septal myectomies performed during the past 40 years. This suggests that many patients have undergone PTSMA before achieving the same symptom (and gradient) threshold advocated for surgical intervention. Part of this enthusiasm for PTSMA derives understandably from the relative ease with which PTSMA can be performed compared with surgery, involving shorter postoperative recovery and less discomfort. However, it should be underscored that even in experienced hands, PTSMA may incur morbidity and mortality similar to that of septal myectomy.

Conclusions

The HCM patient presented here experienced severe disabling symptoms (refractory to medical management), judged to be due to marked LV outflow obstruction. His prior bypass surgery (and postoperative complications) made him an undesirable candidate for septal myectomy. He accepted the PTSMA option and 1.5cc of alcohol were infused into a proximal septal perforator, resulting in a peak creatine phosphokinase of 750U/L. There were no complications other than transient complete heart block requiring temporary pacing for 2 days; he was discharged 5 days after ablation. Six months later, a substantial reduction in outflow gradient (from 65 to 10 mm Hg) was evident, and he became virtually asymptomatic. The patient is being monitored at regular intervals for changes in symptoms, outflow gradient, and arrhythmias. Such cases support the benefit of PTSMA in selected patients with obstructive HCM.

References


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