Alcohol Septal Ablation in Hypertrophic Obstructive Cardiomyopathy
The Need for a Registry

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Familial hypertrophic cardiomyopathy is a genetic disease with an autosomal-dominant inheritance. Patients with this illness are prone to sudden death, angina, syncope, and heart failure. A subset of patients with familial hypertrophic cardiomyopathy have left ventricular outflow tract obstruction (or hypertrophic obstructive cardiomyopathy [HOCM]) at rest or HOCM that can be induced with the Valsalva maneuver or with dobutamine, isoproterenol infusion, or amyl nitrate inhalation. Patients with significant obstruction have systolic anterior motion of the mitral valve associated with the outflow obstruction, which leads to mitral regurgitation. In association with the hemodynamic burden caused by left ventricular outflow tract obstruction, other abnormalities also contribute to the disabling symptoms. These include impaired left ventricular diastolic and systolic dysfunction, myocardial ischemia, and arrhythmias. In some variant patterns, the level of obstruction may be in the mid-left ventricular cavity rather than subaortic. In addition, midventricular obstruction may be associated with subaortic obstruction. With all these abnormalities of ventricular function, the disease is frequently disabling and progressive.

Numerous treatment options have been suggested for HOCM. The primary aim of medical therapy is relief of left ventricular outflow tract obstruction; this is often done using medications such as β-blockers, calcium channel blockers (especially verapamil), and disopyramide. Medical therapy benefits many patients and allows them to lead acceptable, productive lives. Frequently, however, high doses of medication produce side effects that resemble the symptoms of HOCM. In the past, cardiac pacing has been suggested as a method of reducing the outflow tract obstruction and improving symptomatology. However, the results of recently reported randomized trials have diminished the enthusiasm for cardiac pacing as a primary therapy for HOCM. For >40 years, the traditional “gold standard” for treating HOCM has been the ventricular septal myotomy-myomectomy of Morrow, which consists of the surgical resection of a small amount of muscle from the subaortic portion of the septum. Follow-up of patients undergoing myotomy-myomectomy surgery has demonstrated that relief of outflow tract obstruction occurs in 70% to 90% of individuals and improves symptoms and outcomes. The results of surgery from several tertiary centers in North America are excellent. However, in its widespread application, left ventricular myotomy-myomectomy is a major operation with significant morbidity and mortality. Dr Ulrich Sigwart first reported selective septal ablation with ethanol in 1995. Since its first report, alcohol septal ablation has been performed in an estimated 800 cases worldwide. Initial results of ethanol septal ablation show relief of symptoms in the majority of patients, low mortality (short-term), rapid recovery, and improvement that has continued over time; however, long-term follow-up is not yet available.

Although ethanol septal ablation can be performed readily in the catheterization laboratory and it seems efficacious, at least in the short-term, surprisingly similar concerns have been raised by 2 sources. These concerns are centered on several areas, one of which is the possible increased incidence of bradyarrhythmias and tachyarrhythmias. Initial results of alcohol septal ablation showed a relatively high incidence of complete heart block requiring permanent pacemakers. The possibility of progressive septal fibrosis with progression of atrioventricular block producing symptomatic bradyarrhythmias has been raised. Because patients with HOCM are prone to ventricular tachyarrhythmias, the addition of a septal infarction may predispose patients to sustained malignant ventricular arrhythmias by producing the substrate for reentrant tachyarrhythmias. This concern regarding a long-term risk of increased sudden death with alcohol septal ablation has led to the suggestion that the procedure not be performed in very young patients. A second concern is that the elimination of the outflow tract obstruction with a myocardial infarction and a subsequent decrease in intraventricular pressure may lead to impaired ventricular function and thinning of the walls, with progressive heart failure.

Finally, concerns about patient selection have been expressed because ethanol septal ablation in HOCM is easily performed, in contrast to left ventricular myotomy-myomectomy; thus, a more easily performed procedure might lead to the selection of patients who are less symptomatic and to injudicious, widespread use of the procedure. Also, it is possible that provocative maneuvers may artificially produce a subaortic gradient and lead to an unwarranted procedure.

In most individuals, hypertrophy is localized initially to the septum. Then, as more obstruction occurs and intraventricular...
pressure increases, concentric hypertrophy develops as a compensatory response.\textsuperscript{19–21} Secondary ventricular hypertrophy is almost always associated with fibrosis, which ultimately leads to progressive heart failure and ventricular arrhythmias.\textsuperscript{22,23} Overwhelming evidence shows that increased ventricular pressure is a very potent stimulus to cardiac growth and hypertrophy.\textsuperscript{21} Furthermore, suggestive evidence indicates that increased fibrous tissue is the culprit substrate responsible for arrhythmias and sudden death.\textsuperscript{21} Thus, it is also possible that the relief of obstruction early in the course of HOCM may prevent or attenuate the development of hypertrophy and fibrosis and their subsequent complications, including sudden death. However, to perform this procedure in the asymptomatic individual with minimal obstruction would require adequate objective evidence of its safety and long-term benefit.

Because the application of ethanol septal ablation in HOCM has been limited to only a few centers worldwide, a multicenter registry has been suggested. In North America, the majority of cases by far have been done by 1 center.\textsuperscript{15,16} Familial hypertrophy has a relatively low prevalence and, because HOCM occurs in only \(\approx 30\%\) of those with the disease, it is unlikely that any 1 center could recruit an adequate number of patients to determine the safety and efficacy of this procedure. The proposed registry would involve multiple sites in multiple countries and use a standardized protocol, which would include strict selection criteria and a standardized battery of tests that would be interpreted before the procedure by a central core facility to ensure a homogeneous patient population to be treated. The essential technical aspects of the procedure would also be established and followed at each site. A website for reporting patient characteristics and results via the Internet plus a centralized core echocardiographic and genetic facility will be established.

The primary aim of the registry would be to ascertain the percentage of individuals in whom the outflow gradient is reduced by 80\% from baseline compared with 3 months and 1 and 2 years after the procedure. Other objectives of this registry would be to determine the incidence of complications immediately after the procedure, the effect of reducing outflow tract gradient on ventricular function at 3 months and 1 and 2 years after the procedure, and to determine the effect of the procedure on the severity of angina, dyspnea, and exercise capacity at 3 months and 1 and 2 years after the procedure. Symptomatic bradyarrhythmias and tachyarrhythmias and sudden death will be reported to the registry via the website for 2 years. In addition, the registry would determine whether the relief of outflow tract obstruction is associated with progression, lack of progression, or regression of hypertrophy. By establishing standardized selection criteria and treatment protocols, the registry would establish the short- and long-term efficacy and safety of alcohol septal ablation over a 2-year period.

### References


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