Percutaneous Transluminal Septal Myocardial Ablation: A Novel, Nonsurgical Treatment for Symptomatic Hypertrophic Cardiomyopathy

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Patients with severely symptomatic hypertrophic obstructive cardiomyopathy (HOCM) have several alternatives when drugs do not help. Surgical septal myotomy-myectomy, though effective, is an open-heart surgical procedure and can be associated with some complications. The less invasive dual chamber pacing has not lived up to its early promise. Percutaneous transluminal septal myocardial ablation (PTSMA) is a relatively simple, less complicated nonsurgical procedure that can provide an effective and sustained relief of left ventricular outflow tract (LVOT) obstruction. Should it gain wider acceptance? [Rev Cardiovasc Med. *2001;2(2):97–102*]

Key words: Hypertrophic obstructive cardiomyopathy • Percutaneous transluminal septal myocardial ablation • Chemical myomectomy • Surgical septal myotomy-myectomy • Dual-chamber pacing

A 49-year-old man was referred for treatment of severely symptomatic hypertrophic obstructive cardiomyopathy.

History

The patient first became symptomatic 5 years ago when he experienced shortness of breath while playing basketball. Prompted by his symptoms, he sought medical attention and underwent a thorough assessment that revealed that he had hypertrophic obstructive cardiomyopathy (HOCM). He was started on beta-blockers, without

much relief of symptoms. One year ago, he suffered a syncopal attack, following a coughing spell. He was taken to a hospital, where an implantable cardioverter defibrillator (ICD) was implanted. Despite the implantation, he continued to have recurrent syncopal episodes, especially provoked by exertion, or hypovolemia.

One episode of syncope led to a closed head injury and intracranial hemorrhage that required him to be hospitalized for a month. Interrogations of the device have never revealed any serious brady-or tachyarrhythmias. The patient did not have any residual neurologic deficit, but because of the risks of recurrent falls, he has since been on disability. In view of recurrent syncope and a significant resting and dynamic left ventricular outflow obstruction (>80 mm Hg), despite adequate doses of beta-blockers and a permanent pacemaker, he was referred to our institution for percutaneous transluminal septal myocardial ablation (PTSMA).

Physical Examination

Physical examination revealed a grade 4/6 ejection systolic murmur that increased in intensity on Valsalva maneuver and diminished on squatting. There was a separate grade 3/6 blowing pansystolic murmur at apex, suggestive of mitral regurgitation (MR). EKG revealed a paced rhythm, and echocardiography confirmed asymmetrical septal hypertrophy, with the septum measuring 1.8 cm, with evidence of systolic anterior motion of a structurally normal mitral valve, grade 3 mitral regurgitation, and a dynamic left ventricular outflow tract (LVOT) gradient ranging between 40 to 120 mm Hg. We concluded that his symptoms were obviously due to severe outflow obstruction rather than arrhythmias, and so he was considered for PTSMA.

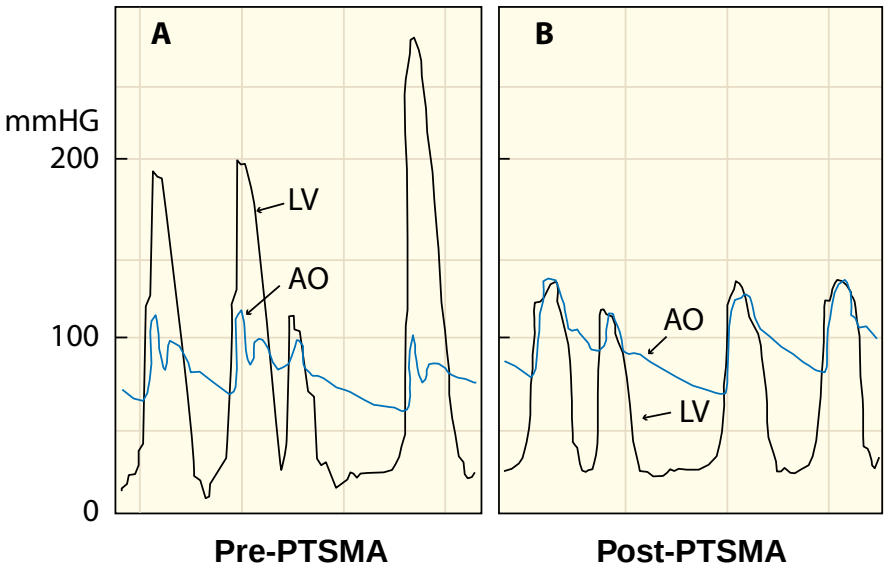

Figure 1. *Simultaneous left ventricle and aortic pressure tracings before and after PTSMA.* ***A.*** *Before PTSMA, there is a significant resting left ventricular outflow tract(LVOT). Note the significant post ectopic potentiation of gradient with reduction of aortic pulse pressure (Brockenbrough-Braunwald phenomenon).* ***B.*** *Post PTSMA, there is a significant reduction of both resting and post ectopic gradient LVOT gradient.*

Procedure

Left-heart catheterization and coronary angiography were performed through the right femoral route in the usual protocol. Simultaneous left ventricle and aortic pressures were recorded with the help of a double lumen pigtail catheter. The mean resting outflow tract gradient measured 66 mm Hg, with postectopic potentiation of 168 mm Hg (Figure 1A). Intraprocedural echocardiography confirmed the findings. The first septal branch of the left anterior descending artery was then identified by selective left coronary angiography, and a 2.0-mm angioplasty balloon was placed in the vessel, over a guidewire. The guidewire was then withdrawn, and the balloon was inflated in the septal branch to 6 atmospheres of pressure-occluded blood flow. A small amount of radio contrast was injected through the central lumen of the balloon catheter into the septal branch distal to the obstruction, delineating the area of myocardium supplied by the vessel, and confirming the absence of spillage of contrast into the main trunk of the left anterior descending artery.

After administration of intravenous Fentanyl for analgesia, 2.5 mL of absolute ethanol was injected slowly over 3 minutes through the central lumen of the balloon catheter into the septal artery. The balloon was deflated after waiting for another 3 minutes following completion of injection of alcohol. Minutes after deflating the balloon, the resting and postectopic left ventricular outflow tract was completely abolished (Figure 1B). Besides minimal chest discomfort during the injection of ethanol, there were no other intraprocedural events. The patient had an uneventful stay in hospital. The peak creatinine phosphokinase

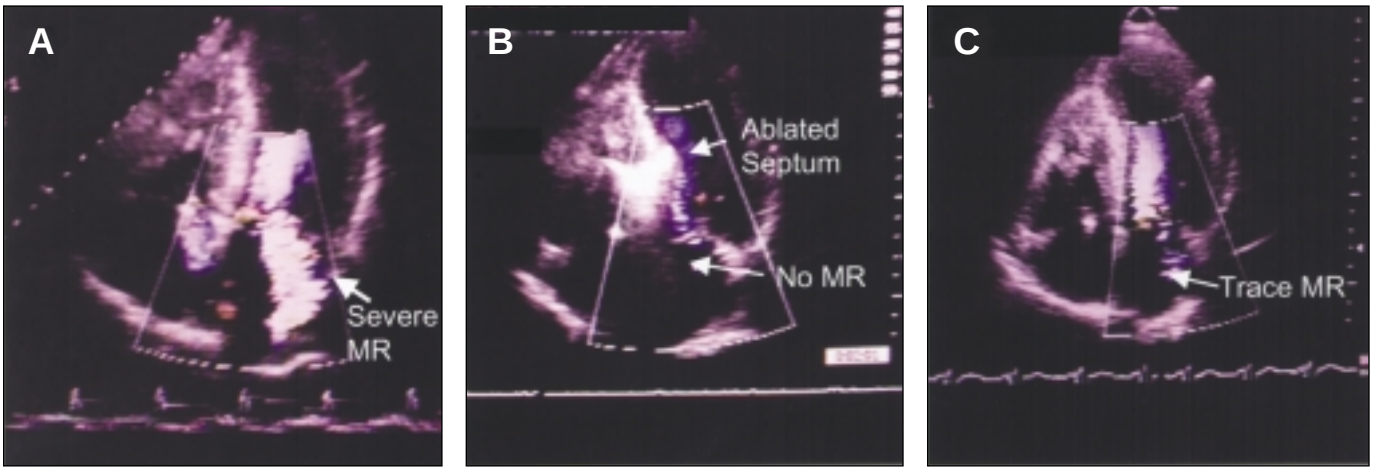

Figure 2. *Changes of mitral regurgitation after PTSMA.* ***A.*** *There is severe eccentric mitral regurgitation(MR) at baseline.* ***B.*** *There is a bright echogenic basal septum just after PTSMA, with no MR.* ***C.*** *Echocardiogram done one day post procedure showing only trace MR.*

activity and peak troponin I level rose to 1305 U/L and 60.8 ng/mL, respectively. Because the patient was in a paced rhythm prior to procedure, it was difficult to determine any new conduction disturbances. Just prior to discharge, physical examination revealed grade 2/6 ejection systolic murmur, and an echocardiogram revealed a non-significant outflow tract gradient, reduced systolic anterior movement of the mitral valve, and just trivial mitral regurgitation (Figures 2A-C). He was discharged 2 days after the procedure.

Follow-Up

The patient has been followed on a regular basis. At his 6-month follow-up visit, he was found to have no further episodes of syncope. He did have some effort intolerance. Echocardiography at this point shows that he continues to have minimal LVOT gradient with only trace mitral regurgitation.

Hospital Experience

Between March 1999 and February 2001, PTSMA was attempted in 17 patients with severely symptomatic HOCM. All patients had a resting gradient >30 mm/Hg, and an inducible gradient >50 mm Hg. The mean age ± SD of the total population was 60.1 ± 15.8 years (range, 33–88 years), with 9 males.

PTSMA was performed successfully in 16/17 patients. Intraprocedural myocardial contrast echocardiography was used to select the target septal artery. The mean resting LVOT gradient decreased from 51.1 ± 29.2 to 14 ± 21.7 mm/Hg, whereas the post ectopic gradient decreased from 122.6 ± 36.3 to 24.7 ± 35.2 mm/Hg. There were no deaths, and two patients required permanent pacemaker implantation for symptomatic trifascicular block.

All patients have been followed up on a regular basis. The median follow up period is 295 days (range, 26 to 442 days). Follow-up echocardiography has shown a sustained reduction of LVOT gradient, except in one patient. Mitral regurgitation improved from an average grade of 2.7 ± 0.8 to 1.3 ± 0.5. The New York Heart Association functional class improved from a grade of 2.9 ± 0.3 to 1.4 ± 0.5.

This ongoing clinical study suggests that PTSMA offers a definite subjective and objective improvement to patients with symptomatic HOCM.

Discussion

Hypertrophic cardiomyopathy is a genetically transmitted myocardial disease that is characterized by unexplained and often severe, asymmetrical hypertrophy of the myocardium.[1,2] A certain subset of patients have an associated dynamic left ventricular outflow tract obstruction (HOCM) that results in an exercise-limiting dyspnea, angina, and exertional syncope. Relief of this obstruction in these symptomatic patients can often be achieved by treatment with beta-blockers or certain calcium channel blockers. In spite of adequate medications, a significant number of patients remain symptomatic with objective of significant dynamic left ventricular outflow obstruction. Such drug-refractory patients often benefit

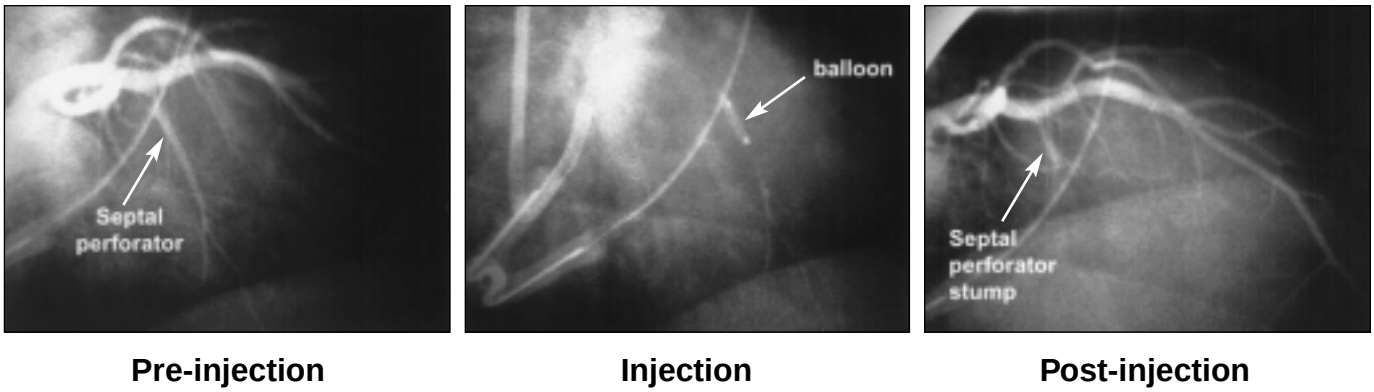

Figure 3. *Coronary angiogram during PTSMA.* ***A.*** *Baseline left coronary angiogram showing a large first septal branch of the left anterior descending artery(LAD).* ***B.*** *Angioplasty balloon catheter in the first septal branch of LAD.* ***C.*** *Post PTSMA left coronary angiogram showing only a stump of the septal branch.*

from surgical septal myotomy-myectomy (Morrow's procedure).[3] The last decade has witnessed the development of several new strategies for the treatment of symptomatic HOCM. One such strategy consists of selectively injecting ethanol selectively into a septal branch of the left anterior descending artery, which results in localized necrosis of the thickened basal septum and thereby relieves the obstruction.[4] This chemical myomectomy, also referred to as PTSMA, leads to significant hemodynamic improvement without recourse to open heart surgery.[4]

In June 1994, Dr. Sigwart injected a small quantity of absolute alcohol into the first septal artery of a 67-year-old woman with symptomatic HOCM.[5] The objective of this rather alarming procedure was to cause a localized infarct in the septum at the LVOT to relieve obstruction, which he successfully accomplished. Furthermore, the production of changes in the electrical activation sequence by altering the conduction system may also explain some of the beneficial aspects of PTSMA. The birth of this procedure was not greeted with widespread enthusiasm by cardiologists. It was difficult to conceive that this "profoundly aggressive" procedure, which would cause a "heart attack," could be beneficial for the patients.[6] In the last 5 years, more than 600 such procedures have been performed, with excellent immediate and mid-term success, and without significant complications.[4,7]

Patients with significant resting and inducible LVOT gradients (>30 mm Hg at rest, and >60 mm Hg under stress) who are severely symptomatic (NYHA Class >III) despite medical treatment are candidates for this procedure.[7] The procedure consists of inflating a small angioplasty balloon in the proximal segment of the first or second septal branch of the left anterior descending artery. The septal branch to be ablated is determined by noting a decrease of gradient while the septal artery is temporarily occluded, or with the help of intraprocedural myocardial contrast echocardiography (MCE). In MCE, a small quantity of echo contrast agent is injected through the lumen of an inflated balloon catheter under continuous transthoracic echocardiographic imaging.

Alcohol is only injected if the areas of maximum flow acceleration and opacified septal myocardium are adjacent to each other.[8] Intraprocedural MCE has been proven to help optimize results as well as reduce the frequency of trifascicular blocks. Once the septal branch has been selected, a small quantity (2 to 3 mL) of absolute alcohol is injected through the central lumen of the balloon catheter slowly at a rate of 1 mL/min into the septal tissue (Figures 3A-C). The balloon is kept inflated during and a few minutes after the completion of the injection, in order to prevent spillage of alcohol into the main trunk of the left anterior descending (LAD) artery. There is usually significant reduction of resting and inducible gradient minutes after the septal ablation. An important technical challenge during this procedure is to avoid spillage of alcohol in the main trunk of the LAD artery. This is prevented by using a slightly oversized balloon, which is kept inflated for a few minutes after completion of injection of alcohol.

Pooled data from a few reported series suggest that this procedure leads to a remarkable early and late clinical and hemodynamic improvement.[8-11] The few studies reporting a long-term follow-up show a rare recurrence of obstruction

with time. The overall published procedural mortality rate is approximately 1% to 2%. These deaths have occurred in elderly patients, one of whom died unexpectedly 10 days after procedure as a result of an unexpected trifascicular block. The most important and frequent complication of this procedure has been the development of transient or permanent trifascicular block. In the initial series,[9,10] a permanent pacemaker was required in 20% to 33% of the cases; however, with the routine use of intraprocedural MCE, as well as the slow injection of alcohol, the incidence of permanent pacemaker use has been dramatically reduced to as low as 7% in some series.[4,8]

There have been no reports of late-onset serious ventricular arrhythmias, ventricular dilatation, or reductions of ejection fraction.

The deliberate creation of a myocardial infarct may create a substrate for arrhythmias and lead to ventricular remodeling. There have been no reports of late-onset serious ventricular arrhythmias, ventricular dilatation, or reductions of ejection fraction. Although this appears encouraging, larger, longer-term follow-up studies are required to reassure the safety of this procedure over time.

The standard strategies used to treat drug refractory HOCM are dual chamber pacing and surgical myotomy-myectomy. Dual chamber pacing, a nonsurgical procedure, initially met with a lot of enthusiasm. However, early widespread enthusiasm has been tempered by the publication of prospective randomized trials that failed to demonstrate convincing objective clinical and hemodynamic improvement with pacing. The role of a placebo effect was raised when these blinded trials only showed modest changes in objective measures of exercise tolerance.[12,13] On the other hand, surgical septal myotomy-myectomy undoubtedly reduces gradient effectively. Unfortunately, this surgical procedure can lead to certain complications and is performed with an acceptable mortality rate (<2%) in only a few experienced centers. Perhaps it is time to compare PTSMA is a prospective manner with surgical septal myectomy and dual chamber pacing for the treatment of symptomatic HOCM.

There is little doubt that this procedure does lead to sustained reduction of left ventricular outflow obstruction.[8-10] There is also evidence from most series that there is a significant and sustained improvement of functional class.[9,14] Objective tests of exercise capacity show an increase in exercise performance over time[9,14]; however these improvements lead to two controversial issues. A first question arises as to whether it is possible to explain the symptomatic benefits from changes in the gradients, and, secondly, the placebo effect of this new procedure cannot be completely discounted. Ideally, these questions could be answered by a double blind, placebo controlled study. However, it is logistically difficult to test this procedure in a rigorous randomized trial. Without such trial, we have to believe from the experienced gained in these studies, that PTSMA leads to improvement of both symptoms and functional class.

Finally, it must be stated that the above-mentioned procedures have been directed primarily to reducing LVOT gradient and have not been shown to alter the natural history of this disease or decrease the overall mortality rate.

In conclusion, it can be stated that echocardiographic-guided PTSMA is an effective nonsurgical strategy for the treatment of symptomatic HOCM with significant LVOT obstruction. The procedure is associated with minimal recurrences and has a low complication rate. Although it is relatively simple, this procedure should be performed only by experienced operators. Larger, long-term prospective studies comparing various strategies to establish the role of this procedure in various subsets of this fascinating disease are ongoing. If carefully nurtured, PTSMA, once considered a "profoundly aggressive" procedure, would prove to be a promising landmark in the palliative treatment of severely symptomatic HOCM. ■

Echocardiographic-guided PTSMA is an effective nonsurgical strategy for the treatment of symptomatic HOCM with significant LVOT obstruction.

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