How to Treat Obstructions in Patients with Hypertrophic Cardiomyopathy

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Abstract

Keywords

- ▶ alcohol septal ablation
- ▶ surgical myectomy
- ▶ hypertrophic cardiomyopathy

Hypertrophic cardiomyopathy (HCM) is characterized by the presence of increased thickness of the left ventricular wall that is not solely explained by abnormal loading conditions. Two-thirds of the patients with HCM have an obstruction in the left ventricle after provocation or even while at rest. This obstruction is associated with more symptoms and a worse prognosis. The two main therapeutic approaches for treating a left ventricular obstruction are alcohol septal ablation and surgical myectomy. Both these techniques are discussed in this article. Currently, the final decision concerning the optimal invasive therapy for patients with obstructive HCM must be individualized to each patient depending on his/her wishes and expectations, way of life, age, heart morphology, and hemodynamics, as well as the experience of the treating center.

Hypertrophic cardiomyopathy (HCM) is characterized by the presence of increased thickness of the left ventricular wall that is not solely explained by abnormal loading conditions.^{1,2} Several observations suggest that the global prevalence of HCM is 1 in every 500 individuals, and some studies have suggested an age-related prevalence that is much higher in patients diagnosed in adulthood.² On the contrary, the occurrence of HCM in the pediatric population is rare. HCM seems to be a rather common genetic malformation of the heart, and more than half of the patients have mutations in the genes encoding sarcomere proteins (β -myosin heavy chain [MYH7], myosin-binding protein C [MYB3], cardiac troponin I and T [TNNT3 and TNNT2], tropomyosin α -1 chain [TPM1], and myosin light chain 3 [MYL3]).^{1,2} Less than 10% of the cases are caused by other disorders, including inherited metabolic and neuromuscular diseases.

HCM is diagnosed based on the imaging methods. It is defined as a left ventricular wall thickness ≥ 15 mm as measured by echocardiography, magnetic resonance, or computed tomography.^{1–3}

The clinical course of HCM varies significantly. Some patients remain asymptomatic throughout their whole lives, some have severe symptomatology of heart failure or angina

pectoris, while others die suddenly even in the absence of previous symptoms. The annual mortality rate depends on the age of patients. The highest mortality rate was demonstrated in young patients in the second decade of life.⁴ In addition, elderly patients have higher mortality than sex- and age-comparable populations, but the risk of sudden death in patients ≥ 60 years of age is low.⁵

Two-thirds of the patients with HCM display evidence of obstruction in the left ventricle after provocation or even at rest (hypertrophic obstructive cardiomyopathy [HOCM]).⁶ This obstruction (≥ 30 mm Hg) is usually based on basal septal hypertrophy, a long anterior and/or posterior mitral leaflet, and systolic anterior motion, which is movement of the anterior mitral leaflet toward the basal segment of the interventricular septum during systole, resulting in a sub-aortic obstruction and pressure gradient between the left ventricle and aorta (► Fig. 1). Systolic anterior motion also results in partial failure of mitral leaflets coaptation, which is typically associated with moderate mitral regurgitation.^{1,2} The other common features of HCM are enlargement of the left atrium, abnormalities in the papillary muscles, hypertrophy of the right ventricle, and the resulting left and right ventricle diastolic dysfunction.

Fig. 1 Transthoracic echocardiography, parasternal long axis. Hypertrophic cardiomyopathy (HCM) with an extremely thickened interventricular septum and systolic anterior motion of the mitral apparatus.

Medical Treatment

The effectiveness of prophylactic treatment has not been tested prospectively. Therefore, we reserve medical therapy only for symptomatic patients.^{1,2} Drug therapy is used as the initial measure for controlling cardiac symptoms that have resulted in functional limitation. It should be emphasized that, in the absence of randomized controlled trials, β -blockers and verapamil have traditionally been administered on an empirical basis, relying on the patient's subjective perception of the benefits. Drug selection is based on the preferences of individual physicians. Most favor β -blockers over verapamil for use in initial treatment, although it is not of critical importance which drug is used first. It is my own experience that β -blockers are often able to decrease the pressure gradient. On the other hand, it should be noted that patients with an obstruction who are treated by verapamil require close monitoring because of its potential to worsen the obstruction with subsequent cardiac failure.

Invasive Therapy

Over the last two decades, technological developments in both surgical and nonsurgical therapies have provided new options for patients with HCM. However, with respect to various clinical courses, symptoms, and anatomies of the left ventricular and mitral morphology, it seems impossible to define the precise guidelines for management. As with many other diseases, it is often necessary to individualize therapy and tailor it for each specific patient. Moreover, there are different practice patterns internationally, with myectomy as the first choice for therapy in the United States and Canada, and alcohol septal ablation (ASA) as the predominant therapy in European countries.^{1-3,7-9} This controversy exists because individual centers favor only one or the other method, and a few have a broad experience with both. Nevertheless, highly symptomatic patients treated by ASA or myectomy are be-

lieved to have better long-term prognosis than similarly symptomatic patients treated conservatively.¹⁰ In addition, there is a firm consensus that both methods are able to improve symptoms and exercise tolerance.¹¹

Generally, symptomatic patients who have a significant outflow gradient greater than 50 mmHg at rest or after provocation and do not respond to medical therapy are the best candidates for surgical or catheter-based therapy.^{1,2}

Myectomy

Based on outstanding reports by cardiothoracic centers mainly in North America, described as "single-center experience papers," myectomy has become the primary therapeutic option for patients with severe symptoms.^{1,2,12-16} Surgical reduction of the outflow gradient is achieved by removing a small amount of muscle (5–10 g) from the basal septum (**Fig. 2**). Recently, some surgeons have performed more extensive myectomies and reconstruction of the subvalvular mitral apparatus. In these cases, the septal myectomy deeply extends into the left ventricular cavity. Subsequently, both papillary muscles are mobilized and all hypertrophied muscular trabeculae are also resected. Authors from the Cleveland Clinic have also demonstrated that it is possible to perform their surgical reorientation, which results in reduction in the left ventricular gradient and subsequent symptomatic relief, in patients with bifid and hypermobile papillary muscles.^{15,16} The findings of long-term surgical studies have shown permanent abolition of the left ventricular obstruction, reduction or even elimination of mitral regurgitation, and relief of symptoms with markedly improved quality of life.¹⁴⁻¹⁶ Furthermore, some data suggest even a reduction in syncope and extended longevity of postmyectomy life that is similar to that of age- and sex-matched general population.¹⁷ Although these single-center results from high-volume hospitals demonstrated that myectomy-related mortality is < 1%, the

Fig. 2 Optimal finding after myectomy.

current evidence from the Nationwide Inpatient Sample database showed a postoperative American mortality rate of 5.9%.¹⁸ This fact again emphasizes the important caveat that replication of outstanding surgical results achieved at the Mayo or Cleveland Clinic is not possible at lower volume centers. In addition, 9% of the patients had to be treated by a permanent pacemaker after myectomy, the average length of hospital stay was 9 days, and the cost of hospitalization was \$41,715.¹⁸ Nevertheless, according to the only ACCF/AHA guideline for the diagnosis and treatment of HCM, surgical myectomy is still the “golden standard” therapy for HOCM.¹

Alcohol Septal Ablation

Ulrich Sigwart published his experience with the “nonsurgical myocardial reduction” of three patients with HOCM in 1995¹⁹ and, at the same time, other centers in Germany also started performing the same interventional procedure.²⁰ It has been shown that injection of a small amount of desiccated alcohol into the first septa branch results in postprocedural necrosis and subsequent basal septal shrinking as a result of myocardial scarring (→ Fig. 3). This intervention is followed by a decrease in the left ventricular obstruction, regression of the left ventricular hypertrophy within the first postprocedural year, improvement of diastolic function, and reduction of the degree of mitral regurgitation. Most importantly, all these changes are accompanied by significant symptom relief.^{3,6–9,21–25} Moreover, in-hospital death, the most significant complication of ASA, is currently < 1%, but in older literature, this ranges from 1 to 4%. However, some newer observations suggest that in skilled hands, the mortality rate is close to zero.^{21–26}

The most important trend in the continuously developing ASA technique involves decreasing the alcohol dose (1–2 mL) injected by very small amounts (0.1–0.3 mL).^{21–23,26} Subse-

Fig. 3 Optimal finding after alcohol septal ablation with thinning of the basal septum.

quent small infarctions are sufficient in reducing obstruction to a similar extent as larger infarctions induced by a higher dose of alcohol. Moreover, it seems likely that a low dose of alcohol is associated with a lower incidence of major postprocedural conduction disturbances and a probability of postprocedural permanent pacemaker implantation of < 10%.^{21–23}

While ASA has not been subjected to randomized clinical trials, observational data from the European and U.S. centers over a 20-year follow-up are consistent, attributing several favorable effects to ASA, which generally parallel that of surgery, including gradual and progressive reduction in outflow gradient over 3 to 12 months and alleviation of symptoms.^{21–27} The most important finding after ASA is an impressive improvement in symptoms during both short- and long-term follow-ups, which is consistently reported by all groups dealing with ASA. The mean functional class improved very significantly from New York Heart Association 2.5–3 to 1.2–1.6.^{21–27} Similarly, objective measurements showed an increase in exercise capacity and peak oxygen consumption. Furthermore, the resting left ventricular outflow tract pressure gradient reduced from 60–70 mm Hg at baseline to 10–20 mm Hg at mid- or long-term follow-up.

There is still a certain gap in the arena of prognosis. In our recent study, the overall annual mortality rate was 2.1%,²⁷ as compared with 3.2% in Bielefeld's study ($n = 644$, mean age at ASA 58 years, mean follow-up 1.4 years),²⁴ 3% in a Scandinavian study ($n = 279$, mean age at ASA 59 years, median of follow-up 3.7 years),²⁸ 2.5% in the Mayo Clinic study ($n = 177$, mean age at ASA 63 years, median of follow-up 5.7 years),²⁹ and 1.2% in a dual-center study performed in Bad Oeynhausen and Copenhagen ($n = 470$, mean age at ASA 56 years, mean follow-up 8.4 years).³⁰ It seems likely that the most important factor influencing post-ASA long-term mortality is a preprocedural patient's selection with regards to comorbidities, which can pose a greater threat to survival than long-standing HCM treated by ASA with the subsequent small and potentially arrhythmogenic scar.²⁷

Conclusion

Currently, for patients with symptomatic HOCM despite medical therapy, myectomy or ASA are justified on symptomatic grounds. In addition, we can speculate that both these therapeutic approaches could be associated with improved prognosis.

Based on the scientific evidence, our own experience, and also common sense, ASA is associated with less discomfort for the patients and this procedure can be performed even in older and surgically high-risk patients. On the other hand, its hemodynamic and clinical results are less predictable. Moreover, the rate of complications after ablation is not negligible.

Surgical myectomy should be performed only in sufficiently trained centers with broadly experienced cardiac surgeons familiar with this technique. In such a case, we can expect acceptable, highly predictive results with permanent abolition of left ventricular obstruction, and also, in some special cases, modification of the mitral valve and papillary muscles.

Moreover, it should be kept in mind that patients with extremely redundant mitral leaflets (sometimes with septal thickness ≤ 18 mm) or anomalous papillary muscles playing a key role in development of the obstruction should be sent to surgical centers.

Further investigation is required to identify the best responders for ASA and surgical myectomy and to compare the results of the available methods. Specifically, a randomized study comparing myectomy and ASA is needed. However, the low incidence of end points would require an extremely high number of participants and, therefore, such a study is probably not feasible.

At the moment, a final decision concerning the optimal invasive therapy of patients with HOCM must be individualized to each patient depending on his/her wishes and expectations, way of life, age, heart morphology, and hemodynamics, as well as the experience of the treating center.

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