Dual chamber pacing for hypertrophic obstructive cardiomyopathy: Has its time come?

Hypertrophic cardiomyopathy, a fascinating and controversial disease, is characterised by massive hypertrophy of the myocardium and is associated with various presentations ranging from complete absence of symptoms to sudden, unexpected death. There is a subgroup of patients who present with severe limiting symptoms of dyspnoea, angina, and syncope related partly to obstruction of the left ventricular outflow tract. Previously, the established therapy for these patients was a trial of β blockers, calcium channel blockers, or disopyramide administered in high doses, followed by septal myectomy for those intolerant of or unresponsive to medications. Recent reports have documented significant symptomatic improvement in many patients with dual chamber pacing, and the question has arisen whether permanent pacemakers should be considered in all patients with hypertrophic obstructive cardiomyopathy who have severe limiting symptoms despite medical treatment.

Pathophysiology of symptoms

It is important to understand the complex pathophysiological processes that contribute to dyspnoea, angina, and syncope in order to direct treatment for patients with hypertrophic cardiomyopathy. Impaired diastolic filling of the left or right ventricle in this condition has long been recognised as a major contributor to the symptoms. Though the documented increase in left ventricular end diastolic pressure was initially believed to be due to increased chamber stiffness caused by the "hypertrophied inelastic muscle" recent insight into the process of ventricular relaxation has led to the conclusion that impaired relaxation may be of greater importance than increased chamber stiffness in explaining abnormalities of diastolic filling. Myocardial relaxation is much impaired in hypertrophic cardiomyopathy and this impairment is believed to be caused by abnormalities of calcium metabolism that lead to abnormal inactivation of the contractile elements, a high systolic contraction load, non-uniformity of relaxation, and myocardial ischaemia. In addition to having severe abnormalities of diastolic function, many patients also have a dynamic left ventricular outflow gradient. Whether this gradient represents true obstruction or is merely a manifestation of rapid early emptying of the hyperdynamic left ventricle has been questioned. Non-invasive Doppler studies have shown true obstruction to outflow. The mechanism of obstruction is said to be the combination of a Venturi effect that draws the anterior mitral leaflet into a narrowed outflow tract and an anatomical anterior displacement of the mitral valve apparatus. The obstruction causes symptoms by placing a systolic over-load on the left ventricle, producing prolonged relaxation and myocardial ischaemia. The displacement of the mitral valve is also responsible for mitral regurgitation, which often occurs and may be important in producing symptoms of dyspnoea. The total contribution from each factor in individual patients is highly variable. The spectrum of pathophysiology probably is wide: some patients have mainly abnormalities of diastolic filling and others have important obstruction of outflow, but most have a combination of the two. Other factors that may contribute to angina and myocardial ischaemia in patients with hypertrophic cardiomyopathy include increased myocardial oxygen requirements by the large muscle mass, high left ventricular diastolic pressures, systolic compression of epicardial arteries, and abnormally thickened small coronary arteries.

Current treatment options

Medical treatment has been directed at improving the pathophysiological abnormalities and has consisted of high dose treatment with β blockers, calcium channel blockers, or disopyramide. In many patients symptoms improve with medical therapy alone. However, a subset of patients is either not able to tolerate the medications at the large doses required or continues to have severe symptoms despite medical treatment. In the United States, these patients who have significant resting or inducible left ventricular outflow gradients have been offered surgical intervention to relieve the obstruction. Currently, transaortic septal myectomy is the operation of choice for relieving obstruction of the left ventricular outflow tract. To preserve conduction tissue in the septum, little septal tissue can be removed at operation. The decrease in the left ventricular outflow gradient is accomplished not only by the physical enlargement of the outflow tract but also by interrupting the physiological sequence of events that cause the outflow gradient. Replacement of the mitral valve with a low profile mitral valve prosthesis—proposed as an alternative to septal myectomy—reduces the left ventricular outflow gradient and improves symptoms. The major problem with this procedure is that one disease process is replaced with another—that is, the problems of durability, infection, thromboembolism, and anticoagulation that are associated with prosthetic valves. Thus transaortic septal myectomy is generally considered to be the most appropriate surgical treatment for patients with hypertrophic obstructive cardiomyopathy and severe symptoms unresponsive to medical therapy. However, there is a significant learning curve to this surgical procedure, and currently the reported experience in the United States is limited to a few centres.
Dual chamber pacing

Recently, dual chamber pacing has been proposed as an alternative to surgical treatment for the relief of symptoms in patients with obstructive hypertrophic cardiomyopathy. Several investigators have independently shown an acute decrease in gradient during atrioventricular sequential pacing (an average decrease of from 82–87 mm Hg to 38–47 mm Hg). Permanent pacing produced considerable symptomatic improvement over short-term follow up. The mechanism responsible is believed to be a decrease in the left ventricular outflow gradient caused by the abnormal septal motion produced by right ventricular pacing. Also there may be a component of ventricular remodelling, as evidenced by ventricular dilatation associated with continued reduction of the gradient found on follow up.3

The idea of a treatment for patients with severe symptoms that does not require open heart surgery is appealing for several reasons. Dual chamber pacing can be performed by all cardiologists and surgeons with pacemaker expertise and does not require specialised referral centres. The risk and cost of a permanent pacemaker are less than those of open heart surgery. The initial encouraging results of dual chamber pacing have led some investigators to recommend a trial of permanent pacing in all patients with severe hypertrophic obstructive cardiomyopathy before proceeding with surgical treatment.

Current results of septal myectomy

Before permanent pacing is recommended to all patients with severe symptomatic hypertrophic obstructive cardiomyopathy, recent results of surgical myectomy from medical centres experienced in this operation must be reviewed. Early reports indicated an operative mortality of up to 14–17% for septal myectomy as well as the complications of heart block, ventricular septal defect, and severe aortic regurgitation. Advances in myocardial preservation techniques and anaesthesia, as well as the key factor of surgical expertise, have greatly improved the surgical results.

Septal myectomy can now be performed with a very low mortality in children and young adults (no deaths in 43 patients) and in patients less than 65 years old (one (1.2%) death in 83 patients). Mortality is higher in older patients and in those undergoing concomitant myocardial revascularisation or cardiac valve procedures. There is proven benefit in relieving outflow obstruction. With myectomy, there is an 87% decrease in gradient, much greater than the 56% decrease in gradient achieved by pacing, and the mean residual gradient is less with surgery (9 mm Hg compared with 38 mm Hg). Mitral regurgitation, when severe, is usually significantly improved after myectomy alone.

From the pathophysiological standpoint, myectomy favourably affects myocardial oxygen consumption and metabolism. Left ventricular end diastolic pressure is significantly decreased, indicating an improvement in overall diastolic filling of the heart. These beneficial changes may occur through several mechanisms, including (a) improvement in ventricular relaxation due to abolition of the high systolic contraction load and relief of ischaemia, (b) decrease in left atrial driving pressure across the mitral valve because of a decrease in mitral regurgitation, and (c) improvement in chamber compliance by relief of ischaemia. Symptomatic improvement is significant, with 90% of patients improving by at least one functional class and 73% being completely free of symptoms on long-term follow up. Although there are no data from randomised trials to examine the effect of myectomy on survival, a 5 year survival rate of 93% has been reported for patients younger than 65 years, which is exceptional for a disease process with 3–4% annual mortality. For patients younger than 40 years, late survival was significantly better than for historical controls.

The prospects

As is true for any new technique, the results of permanent pacing for hypertrophic obstructive cardiomyopathy must be comparable with those of accepted techniques before universal recommendations can be made. The experience with dual chamber pacing in patients with hypertrophic obstructive cardiomyopathy is limited. The decrease in gradient achieved by pacing is modest compared with that provided by surgical myectomy, and its effects on myocardial ischaemia and the stimulus for hypertrophy are unknown. The relatively high residual gradient may be important for these patients: a residual gradient >15 mm Hg was an independent predictor of mortality after surgical myectomy. It is not known how dual chamber pacing affects the degree of mitral regurgitation, which contributes substantially to symptoms of dyspnoea in many patients. The overall effect of dual chamber pacing on diastolic filling of the heart is unknown. Diastolic dysfunction, primarily caused by abnormalities of relaxation, is believed to be important in the pathophysiological process, and right ventricular pacing alone actually prolongs the rate of left ventricular relaxation. We have only short-term follow up on a small number of patients and do not know whether the initial haemodynamic or symptomatic benefit will be sustained in the long term. There may be some unrecognised, harmful adaptation with sustained dual chamber pacing. The ventricular dilatation noted on short-term follow up after pacing may be beneficial initially but in the long term may be detrimental, because eventual ventricular dilatation and heart failure are other causes of death in these patients.

Thus prospective studies to evaluate the efficacy of dual chamber pacing need to be performed before this treatment is used universally in patients with severely symptomatic hypertrophic obstructive cardiomyopathy. The effect of dual chamber pacing on the other pathophysiological mechanisms in patients with this disease must be better understood. Until long-term results of well performed prospective studies are available, surgical myectomy, performed at medical centres with suitable experience, should remain the preferred treatment for most patients with hypertrophic obstructive cardiomyopathy and severe symptoms that are unresponsive to medical treatment.

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