The initial descriptions of hypertrophic cardiomyopathy (HCM) focused on the presence of left ventricular (LV) outflow tract obstruction as a defining feature of the condition.1-6 The use of echocardiography, which emerged as the gold standard technique for non-invasive assessment of the heart from the 1970s onwards, subsequently suggested that only a minority of patients have evidence of LV outflow tract obstruction at rest.7,8 However, more recent studies have shown that up to 70%-75% of patients with HCM have obstruction either at rest (25%-30%) or upon provocation.9,10 This observation has important clinical implications. First, it is well recognized that LV outflow tract obstruction can cause symptoms, including exertional dyspnoea, angina, and syncope or presyncope, resulting from acute reductions in cardiac output, with elevated left ventricular filling pressures and myocardial ischaemia. Symptoms in obstructive HCM are most commonly exertional therefore, the non-invasive evaluation of LV outflow tract obstruction should include provocation manoeuvres such as upright exercise or Valsalva. Furthermore, patients with LV outflow tract obstruction have worse overall, HCM-related and sudden death-free survival than those without obstruction.11-13 The abolition/reduction of LVOTO, and the relief of symptoms associated with it, is therefore a key feature of the management of patients with HCM.

**Mechanism of Left Ventricular Outflow Tract Obstruction**

Our understanding of the mechanisms that result in obstruction to the LV outflow in HCM has evolved substantially over time.14 Initial theories that obstruction was the result of a muscular ring that contracted during ventricular systole15,16 were subsequently disproved; the advent of M-mode echocardiography identified systolic anterior motion (SAM) of the mitral valve as a key feature of obstructive HCM.4 The mechanisms for this phenomenon, however, have been the subject of debate over the past 20 years. Until recently, the most widely accepted explanation for SAM has been that septal hypertrophy and narrowing of the LV outflow tract result in a high velocity zone anterior to the mitral valve that causes its tip to be sucked against the septum by the Venturi effect.17 This hypothesis, however, does not explain a number of features associated with SAM; in particular, the fact that it begins before aortic valve opening and that it can occur in patients with little or no septal hypertrophy. More recent data suggest that, as a result of septal hypertrophy, flow from the ventricular cavity to the outflow tract occurs across the mitral valve, therefore driving it rather than sucking it into the septum.18 In this model, anterior displacement of the papillary muscles and sub-mitral apparatus are necessary to create sufficient leaflet slack to allow the mitral leaflets to move forward in systole.

**Current Treatment Strategies for Obstructive Hypertrophic Cardiomyopathy**

The management of LV outflow tract obstruction in patients with HCM is directed towards the relief of lifestyle-limiting symptoms.19 Pharmacological therapy is the mainstay of treatment for symptomatic LV outflow tract obstruction and often produces adequate results. However, symptoms remain in a small proportion of patients, requiring invasive alternative strategies. The gold standard therapy for symptomatic outflow tract obstruction refractory
to medical treatment is surgical myectomy. In the hands of experienced centres, this procedure results in near or complete abolition of the LV outflow tract gradient in over 90% of patients, with low morbidity and mortality rates of less than 1%.\textsuperscript{13,20} Furthermore, recent observational data suggest a survival benefit in patients who have undergone surgical myectomy compared with those whose LV outflow tract obstruction has been managed without surgery.\textsuperscript{13} A less invasive alternative to surgical myectomy is percutaneous transcatheter alcohol septal ablation, first described in 1995.\textsuperscript{21} Compared to surgical myectomy, symptom relief and gradient reduction with alcohol septal ablation are similar, but complication rates (particularly complete heart block, requiring implantation of permanent pacing systems) and mortality are higher.\textsuperscript{22-26} In patients under the age of 65 years, recurrence of symptoms and mortality rates are almost doubled compared with surgical myectomy patients.\textsuperscript{27}

**Role of Dual Chamber Pacing in Obstructive Hypertrophic Cardiomyopathy**

The potential beneficial effects of pacing in patients with hypertrophic obstructive cardiomyopathy were first reported in the late 1960s and early 1970s.\textsuperscript{28-30} In these reports, right ventricular pacing reduced the LV outflow tract gradient, but at the expense of a drop in systolic aortic pressure and stroke volume. Subsequent studies using atrio-ventricular sequential pacing showed better haemodynamic results,\textsuperscript{31} associated with improved functional capacity in some patients.\textsuperscript{32} However, it was not until Jeanrenaud and colleagues' study in 1992, evaluating the acute and medium-term effects of dual chamber pacing in 13 patients with symptomatic obstructive HCM refractory to pharmacological treatment,\textsuperscript{33} that pacemaker therapy emerged as a potential treatment for symptomatic obstructive disease. In this study, dual chamber pacing significantly reduced LV outflow tract gradient with no change in aortic pressure or cardiac output, and over a follow-up period of up to 62 months, pacing resulted in a significant reduction in symptoms (chest pain and dyspnoea). The proposed mechanism for the beneficial effects of pacing was apical pre-excitation, resulting in attenuated septal contraction and delaying the onset of mitral leaflet-septal contact. The atrioventricular interval was identified as the key factor, needing to be long enough to allow optimum LV filling but shorter than the native atrioventricular interval to preserve apical pre-excitation. This landmark report was followed by other single-centre series that confirmed the acute and longer-term reduction in LV outflow gradients and symptomatic improvement.\textsuperscript{34} However, 3 subsequent multi-centre randomized crossover trials produced less promising results.\textsuperscript{35-37} Although all 3 studies showed a modest reduction in LV outflow tract gradient and subjective symptomatic improvement in some patients, this was not accompanied by objective improvements in cardiovascular performance and mean residual gradients were above 30 mm Hg. Furthermore, a substantial placebo effect was documented in all 3 studies.\textsuperscript{36-38} As a result, pacemaker therapy was relegated to class IIb indication for the treatment of obstructive HCM, and attention was turned to percutaneous alcohol septal ablation as a potential alternative to surgical myectomy. The results of the elegant long-term study by Sandin M et al reported in this issue of Revista Española de Cardiología\textsuperscript{39} appear to support the limited role of pacemaker therapy in the management of obstructive HCM. In keeping with the multicentre trials, although there was a reduction in the LV outflow tract gradient with pacing, this only translated into a subjective symptomatic improvement in less than half the patients, and there was no concomitant improvement in objectively assessed functional capacity. However, pacing remains an attractive therapeutic strategy, given its minimally invasive nature and substantially lower rate of procedure-related morbidity and mortality compared to surgery and transcatheter therapies. In addition, as pointed out by Sandin M et al in this issue,\textsuperscript{39} expertise in surgical and transcatheter gradient reduction procedures is not universal, whilst pacemaker implantation is more widely available. A small subgroup of older patients do appear to show objective improvements in functional capacity,\textsuperscript{36} a finding supported by a recent 10-year follow-up study from Hospital Universitario Vall d’Hebron, Barcelona, of 50 patients with a mean age of 62 years, which showed a significant gradient reduction, subjective and objective improvements in cardiovascular performance, and better health-related quality of life.\textsuperscript{40} Therefore, although not the first-line treatment for LV outflow tract obstruction in HCM, dual chamber pacing does remain a useful therapy for patients at very high risk for surgical or transcatheter therapy, or in whom these options are not available.

**Future Directions**

The 50 years since the initial description of obstructive HCM have seen dramatic improvements in the assessment and management of LV outflow tract obstruction.\textsuperscript{41} Nevertheless, the goal of treatment remains the same: the relief of symptoms and improvement in quality of life. Any novel treatment for obstructive HCM, therefore, must produce significant reduction in subjectively assessed symptoms and objectively assessed cardiovascular
performance. In addition, procedure-related morbidity and mortality should be low. Dual chamber pacing is the only therapy for HCM to have been subjected to rigorous, placebo-controlled randomized trials, with less than promising results. Current data suggest that older patients with mild, localized septal hypertrophy or angulated septa are those most likely to benefit from pacing. Data do not suggest, however, that any other specific subgroups will benefit.

REFERENCES