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Editorial Comment

Appraisal of Dual-Chamber Pacing Therapy in Hypertrophic Cardiomyopathy: Too Soon for a Rush to Judgment?*

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Hypertrophic cardiomyopathy is a primary cardiac disease characterized by a vast clinical and morphologic spectrum (1). Some patients develop disabling symptoms of exertional dyspnea, fatigue and chest pain unresponsive to pharmacologic agents. Functional impairment may result from a number of pathophysiologic mechanisms, most frequently involving left ventricular diastolic dysfunction, but also myocardial ischemia, arrhythmias and dynamic obstruction to left ventricular outflow (1,2).

Historical perspectives. Recently, there has been interest in the application of pacing technology to those patients with hypertrophic cardiomyopathy demonstrating marked outflow obstruction and severe drug-refractory symptoms of heart failure (3–5). Pacing has been advocated as a possible alternative to surgical intervention (ventricular septal myotomy–myectomy or mitral valve replacement), which at present represents the standard treatment approach for such patients (1,2). This therapeutic concept was first proposed in the 1970s in Germany (6) and subsequently in France (7). Subsequently, in 1988, McDonald et al. (8) described symptomatic benefit associated with permanent dual-chamber pacing in 11 patients. Four years later, Swiss investigators (3) demonstrated partial reduction in basal outflow gradient with temporary and permanent pacing, as well as subjective improvement in symptoms. Subsequently, a report of 84 patients (4) attributed multiple benefits to dual-chamber pacing, including a marked symptomatic improvement in virtually all patients, associated with striking reduction in gradient and a striking decrease in left ventricular mass over a brief follow-up period of 2 years. It should be emphasized that these previous reports (3,4) largely reflect a subjective improvement in symptoms outside the context of controlled or randomized study designs. Indeed, objective testing of exercise capacity before and after pacemaker implantation in hypertrophic cardiomyopathy has demonstrated only modest prolongation of exercise time, a finding seemingly inconsistent with the magnitude of subjective improvement reported (4,9). Finally, recent preliminary reports have demonstrated more highly variable patient responses to pacing and are much more restrained in their advocacy of this treatment in patients with hypertrophic cardiomyopathy (10–14).

Most recent observations. In this issue of the Journal, Nishimura et al. (15) at the Mayo Clinic offer an important perspective on this controversy by critically examining the effects of dual-chamber pacing on left ventricular systolic and diastolic function in 29 patients with hypertrophic cardiomyopathy. These investigators prospectively studied the acute hemodynamic effects of P-synchronous pacing at cardiac catheterization by combining high fidelity pressure recordings and pulsed Doppler transmitral flow-velocity measurements. Transseptal catheterization avoided catheter entrapment and ensured more accurate measurement of left ventricular systolic pressure from the inflow portion of the chamber (2).

Within their study design, the authors were able to show hemodynamic deterioration in several key variables as a consequence of pacing. With respect to diastolic function, a significant increase in both the time constant of ventricular relaxation and left atrial pressure were identified during pacing compared with that during periods of sinus rhythm, contrary to a previous suggestion that pacing may benefit patients with hypertrophic cardiomyopathy by enhancing diastolic function (9). In terms of systolic performance, pacing-related decreases in cardiac output and peak positive dP/dt were demonstrable. Each of these hemodynamic alterations was evident at the optimal atrioventricular (AV) delay (defined as the longest interval with maximal pre-excitation, i.e., full ventricular activation by the pacemaker), but were of even greater magnitude at the shortest delay of 60 ms, an interval within the range used in some previous studies (3,8,9).

Of note, Nishimura et al. found only a modest decrease (~15%) in the left ventricular outflow tract gradient with temporary dual-chamber pacing at optimal AV delay, contrasting sharply with the more substantial reductions in gradient reported in previous studies (4,9), and far more modest than the normalization of intraventricular pressures routinely achieved with operation in this disease (1,2,13,16). Furthermore, this response of the gradient to pacing proved to be nonuniform, with some individual patients showing no change or even an increase in outflow obstruction. It is possible that previous studies, in which transseptal catheterization and high fidelity catheters were not used, may have overestimated the magnitude of left ventricular systolic pressure due to the phenomenon of cavity obliteration. Therefore, Nishimura et al. (15) have appropriately addressed a number of issues, including the critical consideration of safety, by emphasizing that pacing therapy in severely symptomatic patients with obstructive hypertrophic cardiomyopathy is not necessarily innocent and may impose a hemodynamic burden with potentially deleterious consequences.

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It should also be noted that the observations of Nishimura et al. (15) were made in the cardiac catheterization laboratory under controlled conditions. Consequently, as the authors themselves concede, some uncertainty persists regarding the extent to which the hemodynamic effects of dual-chamber pacing observed in such a laboratory setting can be extrapolated to clinical circumstances encountered with permanent pacemaker implantation. On the other hand, acute hemodynamic studies, such as those described by Nishimura et al., may be useful as screening procedures from which to judge the prudence of permanent pacemaker implantation in patients with evidence of impaired left ventricular performance during temporary pacing.

Current perspectives. It is also worthwhile to emphasize, in the interest of perspective, that the ongoing debate over pacing in hypertrophic cardiomyopathy is, in reality, focused on a relatively small subgroup of patients with this disease—those with both marked obstruction to left ventricular outflow and severe symptoms of heart failure refractory to drug treatment. Indeed, it is estimated that this subset of patients probably comprises only 5% to 10% of the overall patient population with this disease (1).

Dual-chamber pacing should not be perceived as a general therapeutic panacea or cure for hypertrophic cardiomyopathy, a complex disease characterized by a greatly hypertrophied, noncompliant left ventricle as well as substantial clinical and pathophysiologic heterogeneity (1,2). For example, at present, pacing has no defined role in diminishing risk for sudden cardiac death, nor in relieving the symptoms of patients with the nonobstructive form of the disease (17). On the other hand, it is possible that particular subgroups of patients may yet be recognized within the broad disease spectrum of hypertrophic cardiomyopathy that could be expected to preferentially derive symptomatic benefit from pacing. Finally, it should also be emphasized that pacing therapy in severely symptomatic patients with obstructive hypertrophic cardiomyopathy cannot necessarily be regarded as routine and indeed may prove challenging with long-term pacemaker maintenance and adjustment of the optimal AV delay often necessary in the pursuit of clinical benefit. Patients can require, even after the institution of pacing, substantial drug therapy or AV node ablation to achieve optimal pacing conditions, thus creating a situation in which it becomes difficult to discern to what extent any perceived clinical benefit may actually be attributable to pacing itself.

Conclusions. The evolving but limited clinical experience with permanent pacing therapy in hypertrophic cardiomyopathy suggests the importance at this time of adopting a measured approach and prudent restraint to the widespread adoption of this potential treatment modality for patients with hypertrophic cardiomyopathy. It would indeed be shortsighted to ignore the time-honored surgical treatment (1,2,13,16) for this disease by premature acceptance of permanent pacing as the primary treatment for refractory symptoms. Therefore, it is perhaps appropriate to sound this cautionary note regarding dual-chamber pacing as a treatment strategy in hypertrophic cardiomyopathy until more definitive information becomes available from the prospective, well controlled and randomized trials currently in progress. Indeed, the present report of Nishimura et al. (15) from the Mayo Clinic should serve as an important stimulus for much needed studies aimed at defining more precisely the true role of dual-chamber pacing in the therapeutic armamentarium of patients with hypertrophic cardiomyopathy.

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