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# Effects of Dual-Chamber Pacing for Pediatric Patients With Hypertrophic Obstructive Cardiomyopathy

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***Objectives.*** **The effects of both temporary and permanent dual-chamber pacing (DCP) were evaluated in symptomatic pediatric patients with hypertrophic obstructive cardiomyopathy (HOCM) unresponsive to medications.**

***Background.*** **Permanent DCP pacing can reduce left ventricular outflow tract (LVOT) gradient and relieve symptoms in adult patients with HOCM.**

***Methods.*** **Ten patients (mean [±SD] age 11.1 ± 6 years, range 1 to 17.5) with HOCM and a Doppler LVOT gradient ≥40 mm Hg were studied. The seven patients showing hemodynamic improvement during temporary pacing at cardiac catheterization underwent surgical implantation of a permanent DCP system. The effects of permanent pacing were evaluated using a questionnaire, Doppler evaluation, treadmill testing and repeat cardiac catheterization.**

***Results.*** **At initial cardiac catheterization, three patients failed to respond to temporary pacing (inadequate pace capture in two; congenital mitral valve abnormality in one). The remaining seven patients (70%, 95% confidence interval 38.0% to 91.7%; mean age 13 ± years, range 4 to 17.5) showed a significant reduction ($p < 0.05$) in LVOT gradient, left ventricular systolic pressure and pulmonary capillary wedge pressure. After pacemaker implantation, these seven patients reported a significant reduction in dyspnea on exertion and exercise intolerance. Serial Doppler evaluation showed a significant reduction in LVOT gradient. Follow-up catheterization at 23 ± 4 months in six patients (one patient declined restudy) showed a persistent decrease in LVOT gradient (53 ± 13 vs. 16 ± 11 mm Hg), left ventricular systolic pressure (149 ± 16 vs. 108 ± 14 mm Hg) and pulmonary capillary wedge pressure (18 ± 2 vs. 12 ± 4 mm Hg) versus preimplantation values.**

***Conclusions.*** **Permanent DCP is an effective therapy for selected pediatric patients with HOCM. Rapid atrial rates and intrinsic atrioventricular conduction, as well as congenital mitral valve abnormalities, may preclude effective pacing in certain patients.**

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Children with hypertrophic obstructive cardiomyopathy (HOCM) present special challenges in management. Unlike adult patients, they have progressive left ventricular hypertrophy, are more likely to die suddenly and frequently present with overt congestive heart failure (1–7). Current treatment of HOCM includes pharmacologic management or surgical resection of obstructing left ventricular outflow tract (LVOT) muscle reserved for nonresponsive patients. These treatment options may have significant side effects and are not believed to alter the natural history of this disorder (3,5,8–15). Less than optimal clinical outcomes using current treatment regimens have led investigators to search for alternate, more effective approaches.

In 1975, Hassenstein et al. (16) performed right ventricular pacing in four adults with HOCM, finding symptomatic improvement and a 56% reduction in LVOT gradient. Over the ensuing years, other investigators (17–20) have reported decreased symptoms and LVOT gradients, as well as improved diastolic function (20,21).

Based on these findings, we speculated that dual-chamber pacing (DCP) may have similar benefits for pediatric patients with HOCM. The specific aim of the present study was to test the following hypotheses: 1) temporary transvenous DCP during cardiac catheterization acutely decreases LVOT gradient; and 2) long-term DCP promotes subjective and objective improvement in pediatric patients with HOCM.

## Methods

**Study patients.** The study group included 10 pediatric patients (1 to 17.5 years old) with an echocardiographic diagnosis of HOCM and a rest Doppler maximal instantaneous gradient ≥40 mm Hg across the LVOT gradient. Patients were chosen without regard to gender, race or ethnic background. The study was approved by the Emory University School of Medicine Human Investigations Committee, and all procedures were performed in accordance with institutional guide-

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**Abbreviations and Acronyms**

AV = atrioventricular
DCP = dual-chamber pacing
ECG = electrocardiogram
HOCM = hypertrophic obstructive cardiomyopathy
LVOT = left ventricular outflow tract

lines. Written informed consent was obtained from all individuals/guardians participating in the study.

**Preevaluation and follow-up schedule.** Before catheterization, each patient completed a questionnaire regarding symptoms and underwent outpatient 24-h Holter monitor, LVOT Doppler evaluation and exercise treadmill testing (all patients ≥8 years age), followed by cardiac catheterization with temporary DCP. After placement of a permanent pacemaker, patients were reevaluated in the pacemaker clinic. During these visits, complete pacemaker analysis and blinded continuous wave Doppler to document LVOT gradient at different pacing rates, modes and atrioventricular (AV) intervals were performed. Twenty-four hour Holter monitoring was repeated at 6, 12 and 18 months, and exercise treadmill testing was repeated at 6 months. Follow-up hemodynamic catheterization to evaluate the long-term effects of permanent DCP was planned at least 18 months after implantation of the pacing system.

**Questionnaire.** Each patient and family was questioned about history of chest pain, shortness of breath, dyspnea on exertion, exercise intolerance, palpitations, dizziness, presyncope and syncope (rating the response as 0 [never] to 5 [always]), as well as the use of any medications. At postimplantation pacemaker clinic visits, patients were specifically asked to grade their present condition as "worse," "unchanged," "improved" or "asymptomatic." A follow-up questionnaire was administered at the time of repeat cardiac catheterization.

**Echocardiography and Doppler.** Complete two-dimensional echocardiography with Doppler was initially performed to analyze structural abnormalities and to document the rest LVOT gradient using a Hewlett-Packard Sonos or 1000 or Sonos 1500 real-time, phased-array ultrasound scanner. Two-dimensional images were obtained in multiple planes using standard transducer positions. Continuous wave Doppler examinations from the apical window were performed and guided by color flow mapping two-dimensional echocardiography to estimate the maximal LVOT gradient. Care was taken to separate the mitral regurgitation signal from that of the LVOT gradient. The LVOT gradient was estimated using a modified Bernoulli equation. After pacemaker implantation, Doppler evaluation was performed in blinded manner with regard to changes in pacemaker rates, modes and AV intervals.

**Holter monitoring.** Twenty-four hour Holter monitoring was performed to assess intrinsic atrial rate variability throughout the day. QRS complexes were assessed for 100% ventricular capture with maximal QRS duration. Holter monitoring also allowed for analysis of any significant atrial or ventricular arrhythmia.

**Exercise treadmill testing.** All patients ≥8 years age underwent treadmill testing using the standard Bruce protocol. Exercise duration, rest and maximal heart rates and blood pressure (using manual blood pressure cuff), and any significant symptoms were documented. The electrocardiogram (ECG) was analyzed to determine whether appropriate atrial tracking, 100% ventricular pacing and capture with maximal pre-excitation were present after pacemaker implantation. Atrial or ventricular arrhythmias, or both, were noted. Doppler evaluation of maximal exercise LVOT estimated gradient was not performed.

**Cardiac catheterization.** Patients received premedication with oral midazolam or diazepam. During the first cardiac catheterization, a combination of midazolam and fentanyl or morphine intravenously was used for sedation and analgesia, respectively. Xylocaine was infused for local analgesia. To determine the effect of DCP, beta-adrenergic or calcium channel blocking agent treatment, or both, was continued in each patient up to the time of catheterization. Hemodynamic data obtained during baseline normal sinus rhythm included left ventricular systolic and end diastolic pressures, aortic pressure, pulmonary artery pressure, pulmonary wedge pressure and thermodilution cardiac output using the Swan-Ganz catheter. Left ventricular pressure was recorded through a retrograde arterial approach, taking care to position the catheter apically and using a pigtail catheter to avoid catheter entrapment with resultant falsely elevated apical pressures. Two 5F quadrapolar electrophysiologic catheters were positioned for pacing at the right ventricular apex close to the interventricular septum and in the right atrial appendage. Temporary DCP with an external Intermedics Relay pacemaker (model 294-03) was performed. Hemodynamic data were remeasured during P-synchronous ventricular pacing and AV sequential pacing at rates of 100 to 120 beats/min with AV intervals of 75 to 125 ms. The shortest AV interval producing right ventricular pre-excitation on the surface ECG with the least LVOT gradient was determined. Pacing was performed 10 min for stabilization before repeat measurement of hemodynamic measures during each mode, rate or AV interval variable change. There were no complications during this temporary pacing procedure.

The second catheterization was scheduled at least 18 months after pacemaker implantation. Patients received premedication with oral midazolam or diazepam, and intravenous midazolam or fentanyl or morphine was given for sedation and analgesia. Complete hemodynamic evaluation was performed as previously described at the patient's current pacemaker mode and timing interval settings. Long-term beta- or calcium channel blocker treatment, or both, was continued up to the time of study.

**Pacemaker implantation.** Seven patients (Patients 1 to 7) underwent implantation of an Intermedics Cosmos II pulse generator (model 284-05). This pulse generator was chosen in view of its capabilities for acquiring and storing diagnostic

**Table 1.** Patient Demographics

| Pt No./ Gender | Previous Rx | Cath 1 | | Cath 2 | |
|---|---|---|---|---|---|
| | | Age | Rx | Age | Rx |
| 1/F | V | 17 yr, 5 mo | BB | 19 yr, 10 mo | BB |
| 2/M | BB,V | 15 yr, 8 mo | 0 | 17 yr, 8 mo | BB |
| 3/M | BB,V | 13 yr, 1 mo | BB | 15 yr, 1 mo | V |
| 4/M | BB,V | 8 yr, 5 mo | BB | 10 yr, 4 mo | BB |
| 5/F | BB | 4 yr, 2 mo | BB | 5 yr, 10 mo | BB |
| 6/M | BB | 17 yr, 6 mo | BB | 19 yr | BB |
| 7/M | BB | 14 yr, 6 mo | BB | — | — |
| 8/F | BB | 1 yr | BB | — | — |
| 9/F | V | 5 yr | V | — | — |
| 10/M | BB,V | 14 yr, 1 mo | BB | — | — |

BB = beta-adrenergic blocking agent; Cath = catheterization; F = female; M = male; Pt = patient; Rx = medical treatment; V = verapamil; — = not applicable.

data, DCP capabilities and highly variable AV interval settings. Six patients had transvenous leads, and one patient (4 years old, Patient 5) underwent implantation of an epicardial system because of her small size; bipolar leads were placed in/on the right atrial appendage and at the right ventricle apex close to the interventricular septum. A special Intermedics programming module allowed a decrease in the AV interval to a minimum of 30 ms.

**Pacemaker analysis.** Pacemaker analysis included assessment of intrinsic rhythm and atrial and ventricular sensing and pacing thresholds. Pacemaker diagnostic data were reviewed for the percentage of the time that the patient was actually paced. Careful adjustments of the AV interval and pacing rates were performed simultaneously with Doppler echocardiography to achieve the least LVOT gradient without mitral inflow obstruction.

**Statistics.** Serial catheterization measurements were statistically analyzed using the Student *t* test for paired data. The Wilcoxon signed-rank test was used for analysis of questionnaire data comparing patient scores before and after pacemaker implantation. Analysis of variance for repeated measures (Bonferroni method) was used to evaluate repeated Doppler estimates of LVOT gradients. A p value $\leq 0.05$ was considered significant. Data are presented as mean value ± SD. Confidence intervals for proportions were calculated using the mid-p exact method (22).

**Table 3.** First Cardiac Catheterization Hemodynamic Variables in Seven Patients

| | BL (mean ± SD) | TP (mean ± SD) | p Value |
|---|---|---|---|
| LV systolic pressure (mm Hg) | 150 ± 15 | 114 ± 13 | < 0.001 |
| Ao systolic pressure (mm Hg) | 97 ± 13 | 105 ± 11 | NS |
| LVOT gradient (mm Hg) | 54 ± 12 | 9 ± 4 | < 0.001 |
| CI (liter/min per $m^2$) | 3.5 ± 1.0 | 3.5 ± 0.8 | NS |
| PCW pressure (mm Hg) | 17 ± 2 | 13 ± 2 | 0.005 |

Abbreviations as in Table 2.

## Results

**Demographics.** Table 1 summarizes age, gender and medications for Patients 1 to 10 (four female, six male; mean age 11.1 ± 6 years, range 1 to 17.5). Each patient had been previously unsuccessfully treated with either beta-blockers (four patients) or calcium channel blockers (two patients), or both (four patients). The diagnosis of HOCM was made by echocardiography, which demonstrated severe hypertrophy of the myocardium (septum or left ventricular free wall) in the absence of an identified etiology. Each patient (except for Patient 2), was receiving concomitant drug therapy at the time of the temporary pacing evaluation. After pacemaker implantation, drug therapy was used in Patients 2 and 6 for treatment of asymptomatic nonsustained ventricular tachycardia and for slowing of AV node conduction in Patients 1, 3 to 5 and 7.

**Baseline cardiac catheterization with temporary DCP.** Seven of 10 patients (70%, 95% confidence interval 38.0% to 91.7%; mean age 13 ± 5 years, range 4 to 17.5) showed hemodynamic improvement during temporary DCP at first cardiac catheterization. Catheterization data (from first and second catheterizations) for these seven patients are reported in Table 2. Compared with baseline sinus rhythm (Table 3), temporary DCP at AV intervals 75 to 125 ms resulted in

**Table 2.** Catheterization Hemodynamic Data in Seven Patients

| Pt No. | LV Systolic Pressure (mm Hg) | | | Ao Systolic Pressure (mm Hg) | | | LVOT Gradient (mm Hg) | | | CI (liter/min per $m^2$) | | | PCW Pressure (mm Hg) | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | BL | TP | PP | BL | TP | PP | BL | TP | PP | BL | TP | PP | BL | TP | PP |
| 1 | 175 | 110 | 130 | 100 | 100 | 104 | 75 | 10 | 26 | 3.0 | — | 3.5 | 19 | 10 | 14 |
| 2 | 134 | 110 | 105 | 90 | 105 | 108 | 44 | 5 | 0 | 2.8 | 3.3 | 3.6 | 18 | 11 | 11 |
| 3 | 140 | 118 | 119 | 100 | 108 | 85 | 40 | 10 | 34 | 3.7 | 3.4 | 2.6 | 20 | 12 | 19 |
| 4 | 140 | 90 | 94 | 82 | 84 | 80 | 58 | 6 | 14 | 4.1 | — | 2.9 | 14 | 11 | 10 |
| 5 | 140 | 118 | 95 | 85 | 114 | 80 | 55 | 4 | 15 | 5.1 | 4.6 | 3.8 | 16 | 14 | 15 |
| 6 | 163 | 130 | 103 | 120 | 120 | 93 | 43 | 10 | 10 | 3.8 | 3.8 | 2.9 | 18 | 17 | 7 |
| 7 | 160 | 120 | — | 100 | 105 | — | 60 | 15 | — | 2.0 | 2.5 | — | 14 | 14 | — |

Ao = aortic; BL = baseline hemodynamic data; CI = cardiac index; LV = left ventricular; LVOT = left ventricular outflow tract; PCW = pulmonary capillary wedge; PP = hemodynamic data during permanent pacing at second catheterization; Pt = patient; TP = hemodynamic data during temporary pacing at first catheterization; — = not applicable.

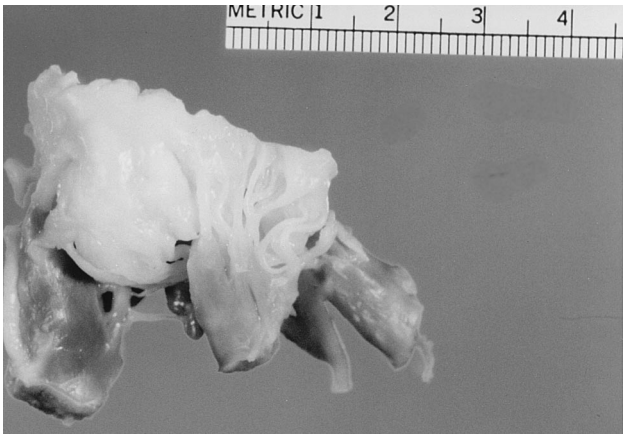


**Figure 1.** Pathologic mitral valve and papillary muscle specimen from Patient 10. Direct papillary muscular insertion into the mitral valve leaflets can be seen.

significantly lower ($p < 0.05$) left ventricular systolic pressure (150 ± 15 vs. 114 ± 13 mm Hg), LVOT gradient (54 ± 12 vs. 9 ± 4 mm Hg) and pulmonary capillary wedge pressure (17 ± 2 vs. 13 ± 2 mm Hg). No change was noted in cardiac index (3.5 ± 1.0 vs. 3.5 ± 0.8 liter/min per $m^2$) or aortic systolic pressure (97 ± 13 vs. 105 ± 11 mm Hg).

Patients 8 and 9 were never satisfactorily or consistently paced during temporary DCP. Both patients had fast sinus atrial rates and rapid AV conduction, despite sedation, and a reliable ventricular-paced pre-excited QRS complex was never achieved. The effects of temporary pacing therefore could not be adequately assessed.

Previous medical trials with both calcium channel and beta-blockers had failed in Patient 10; temporary DCP did not reduce the LVOT gradient. After catheterization, further review of his echocardiographic evaluation indicated a congenital mitral valve abnormality (Fig. 1), defined as upward displacement of the hypertrophied mitral valve papillary muscles into the LVOT gradient, with direct anomalous insertion of the mitral valve papillary muscles into the valve leaflets, without intervening chordae tendinae (23). This patient was referred for mitral valve replacement, which eliminated the LVOT gradient.

**Left ventricular outflow tract gradient Doppler evaluation.** Table 4 summarizes LVOT gradient Doppler evaluation for Patients 1 to 7. Preimplantation Doppler estimates of LVOT obstruction form the basis for serial comparison to subsequent outpatient Doppler evaluations during pacemaker reprogramming. Doppler evaluations are reported for 1-week and 1-, 3-, 6-, 12- and 18-month intervals after implantation. For Patient 4, Doppler evaluation predicted a LVOT gradient 17% above the baseline value at his 1-week evaluation; review of the ECG showed that his programmed AV interval was too long to achieve a widely pre-excited QRS complex. After reprogramming of his AV interval, he subsequently demonstrated a decrease in his Doppler predicted LVOT gradient.

At 1-week Doppler gradients had decreased significantly ($p < 0.05$) compared with baseline data. Subsequent Doppler evaluation of the LVOT predicted gradient showed no appreciable change over the remaining 17 months of our evaluation.

**Table 4.** Doppler Left Ventricular Outflow Tract Gradient Evaluation

| Pt No. | Left Ventricular Outflow Tract Gradient (mm Hg) | | | | | | |
|---|---|---|---|---|---|---|---|
| | BL | 1 wk | 1 mo | 3 mo | 6 mo | 12 mo | 18 mo |
| 1 | 64 | 8 | 20 | 8 | 8 | 6 | 12 |
| 2 | 55 | 15 | 14 | 13 | 16 | 15 | 15 |
| 3 | 40 | 15 | 11 | 13 | 13 | 10 | 14 |
| 4 | 77 | 90 | 43 | 35 | 12.5 | 36 | 15 |
| 5 | 50 | 16 | 15 | 16 | 25 | 10 | 25 |
| 6 | 51 | 13 | 9 | 10 | — | 11 | 10 |
| 7 | 72 | 20 | 24 | 28 | 36 | 36 | — |
| Mean | 58.0 | 25.0* | 19.4* | 17.6* | 18.4* | 17.7* | 15.2* |
| SD | 13.0 | 28.8 | 11.6 | 10.0 | 10.3 | 12.8 | 5.2 |

*$p < 0.05$ versus baseline Doppler evaluation before implantation. Abbreviations as in Table 2.

**Exercise treadmill testing.** Patients 1 to 4 and 6 and 7 underwent serial treadmill testing. Maximal heart rate response before pacemaker implantation was 167 ± 14 versus 170 ± 13 beats/min after pacemaker implantation, not significantly different. Total exercise time (Table 5) before implantation was 8.0 ± 1.8 versus 9.9 ± 1.8 min after implantation ($p < 0.05$). No patient had exercise-induced ventricular or supraventricular tachycardia. Several patients showed an occasional decrease in the width of their ventricular-paced QRS complex at upper exercise heart rates, due to competition with enhanced AV conduction at maximal exercise. Doppler interrogation of the LVOT at maximal exercise was not performed.

**Pacemaker diagnostic data and Holter monitoring.** When optimally programmed (AV intervals 60 to 110 ms), no patient showed <98% ventricular paced complexes with either AV sequential or P-synchronous ventricular pacing. Holter monitoring was used in conjunction to verify that the paced QRS complexes were widely pre-excited secondary to control of ventricular activation by the pacemaker.

**Table 5.** Exercise Treadmill Time Before and After Permanent Dual-Chamber Pacing

| Pt No. | Total Exercise Time (min) | |
|---|---|---|
| | Preimplantation | Postimplantation |
| 1 | 6.3 | 7.6 |
| 2 | 5.8 | 8.7 |
| 3 | 7.4 | 9.6 |
| 4 | 8.7 | 11 |
| 5* | NA | NA |
| 6 | 10 | 12.6 |
| 7 | 10 | 10 |
| Mean | 8.0 | 9.9 |
| SD | 1.8 | 1.8 |

*Patient (Pt) 5 did not undergo permanent treadmill evaluation because of young age. NA = not applicable.

**Table 6.** Second Cardiac Catheterization Hemodynamic Variables in Six Patients

| | BL (mean ± SD) | TP (mean ± SD) | PP (mean ± SD) | p Value BL–TP | p Value BL–PP | p Value TP–PP |
|---|---|---|---|---|---|---|
| LV systolic pressure (mm Hg) | 149 ± 16 | 113 ± 13 | 108 ± 14 | 0.002 | < 0.001 | NS |
| Ao systolic pressure (mm Hg) | 96 ± 14 | 105 ± 13 | 92 ± 12 | NS | NS | NS |
| LVOT gradient (mm Hg) | 53 ± 13 | 8 ± 3 | 16 ± 11 | < 0.001 | < 0.001 | NS |
| CI (liter/min per $m^2$) | 3.8 ± 0.8 | 3.8 ± 0.6 | 3.2 ± 0.5 | NS | NS | NS |
| PCW pressure (mm Hg) | 18 ± 2 | 13 ± 3 | 12 ± 4 | 0.004 | 0.03 | NS |

Abbreviations as in Table 2.

**Radiofrequency ablation.** Patient 5 underwent AV node radiofrequency ablation without complication, after outpatient ECG evaluation repeatedly revealed inadequate ventricular paced pre-excitation associated with worsening symptoms. Shortening of the programmed AV interval to 30 to 50 ms had acutely resulted in pulmonary edema immediately after pacemaker implantation, but at longer programmed AV intervals, rapid intrinsic AV node conduction prevented rapid maximal pacing benefits.

**Questionnaire data.** Six patients and their parents completed serial questionnaires; Patient 7 declined the follow-up questionnaire. Before and subsequent to pacemaker implantation, no patient complained of presyncope, and no patient had experienced syncope or sudden death episodes. After implantation, each patient was judged by himself/herself and parents as symptomatically "improved." Chest pain and palpitations were uncommon complaints before pacemaker implantation and were not significantly improved subjectively by pacemaker implantation. In contrast, significant ($p < 0.05$) improvement was seen in both dyspnea on exertion (3.5 vs. 0.5, median score) and exercise intolerance (3.5 vs. 0.5, median score). Patients 1 to 3 each improved symptomatically enough to participate in neighborhood aerobic, low intensity sports (tennis, softball). Patient 5 showed a dramatic decrease in pulmonary symptoms (frequently requiring hospital admission) attributed to pulmonary venous congestion.

**Follow-up catheterization.** The second catheterization was performed 23 ± 4 months after pacing system implantation in six of seven patients (Patient 7 declined reevaluation). Age at reevaluation was 14.6 ± 5.5 years. Each patient was paced in the DDD mode, with pacing rates from 80 to 120 beats/min AV intervals programmed from 75 to 110 ms. Results were similar to the temporary pacing hemodynamic findings noted earlier in this group of six study patients (Table 6). Sustained significant ($p < 0.05$) decreases (compared with preimplantation values) in left ventricular systolic pressure (149 ± 16 vs. 108 ± 14 mm Hg), left ventricular outflow gradient (53 ± 13 vs. 16 ± 11 mm Hg) and pulmonary capillary wedge pressure (18 ± 2 vs. 12 ± 4 mm Hg) were measured. Aortic systolic pressure (96 ± 14 vs. 92 ± 12 mm Hg) and cardiac index (3.8 ± 0.8 vs. 3.2 ± 0.5 liters/min per $m^2$ were unchanged. No statistical differences were noted in any of the five measured hemodynamic indexes between temporary pacing evaluation and the subsequent follow-up pacing catheterization.

## Discussion

**Main findings.** The present study demonstrates that permanent DCP can decrease symptoms, increase exercise time and improve hemodynamic variables in children with HOCM who show therapeutic response to temporary DCP. Temporary DCP in 7 (70%) of 10 patients (95% confidence interval 38.0% to 91.7%) significantly decreased left ventricular pressure, LVOT gradient and pulmonary capillary wedge pressure; this acute change was sustained, both as assessed by noninvasive Doppler evaluation during pacing analysis and at follow-up cardiac catheterization 23 months later. The reduction in LVOT gradient is consistent with hemodynamic data from adult studies (17–20,24).

Importantly, each of these seven patients had been symptomatic with LVOT Doppler gradients >40 mm Hg despite the use of medications before pacemaker implantation. Individually, each patient reported symptomatic improvement, confirmed by parents. Exercise treadmill time was increased significantly for the group, and each patient tested serially, except Patient 7, showed an increase in total treadmill exercise duration. Serial questionnaires were administered to patients and their parents to more accurately define symptomatic change, fully realizing the difficulty quantifying symptoms in young children and possible placebo effect of DCP. Other investigators have noticed subjective symptomatic improvement with DCP, despite only modest (though significant) increases in exercise times (19,20). No studies have reported the evaluation of exercise-related gradients after pacemaker implantation; it is possible that pacing may improve symptoms during exercise by relieving exercise-induced LVOT obstruction.

**Effects of pacing on diastolic function.** Debate still continues about the impact of DCP on diastolic function in patients with HOCM. Diastolic dysfunction contributes greatly to the symptoms in the majority of patients with HOCM. Diastolic filling of the left ventricle is a complex sequence of many interrelated events, each of which is difficult to accurately measure in the beating heart. Duch et al (21) and McDonald and Mauer (20) have shown a beneficial effect of pacing on diastolic function, consistent with our data showing a decreased pulmonary capillary wedge pressure reflecting a decrease in left ventricular end-diastolic pressure. The exact physiologic mechanism causing the decrease in pulmonary

capillary wedge pressure with pacing is incompletely understood. In contrast, Bettocci et al. (25) reported impaired diastolic function during AV pacing, as evidenced by increased pulmonary capillary wedge pressure during AV pacing in 16 patients with hypertrophic cardiomyopathy. These investigators demonstrated that although AV pacing did relieve LVOT obstruction in patients with HOCM, diastolic function was impaired, as shown by the prolongation of the time constant of isovolumetric relaxation despite the decrease in left ventricular systolic pressure and a decrease in peak filling rate despite the elevation of pulmonary capillary wedge pressure. The acute Doppler echocardiographic and catheterization hemodynamic study by Nishimura et al. (24) reported deterioration of diastolic function variables during pacing, greater at short AV intervals than at long AV intervals. The shortest AV interval evaluated (60 ms) in their adult patients was shorter than the optimal AV interval in our pediatric patients; in these patients left atrial pressure was increased, presumably due to atrial contraction against a closed mitral valve. They also reported a significant, though modest, decrease in LVOT gradient from $73 \pm 45$ to $61 \pm 41$ mm Hg ($p < 0.05$) during DCP at optimal AV delay.

**Importance of paced AV interval.** Benefits to patients with HOCM accrue from permanent DCP presumably because of a change in septal activation by the right ventricular pacing (17,18,20), although still maintaining AV synchrony. Many studies, including Nishimura et al. (24), have emphasized the critical impact that the appropriate AV interval has on the success of this treatment modality. Patients may often require, even after the institution of pacing, concomitant drug therapy or AV node ablation, or both, to achieve optimal pacing conditions. Determination of the optimal AV delay may prove to be especially time-consuming and difficult in pediatric patients with more rapid intrinsic AV conduction. Selection of a newer generation of implanted pacemaker with rate-adaptive AV intervals may allow for custom tuning of AV intervals to provide widely pre-excited paced QRS complexes both at rest and during exercise.

**Ventricular remodeling.** Reduction or elimination of chronic LVOT obstruction by DCP theoretically could cause regression of left ventricular and septal hypertrophy secondary to the outflow obstruction itself, without affecting the primary cardiomyopathic process itself. This remodeling has been espoused by Fananapazir et al. (19). Due to the varied morphologic presentation of HOCM with asymmetric hypertrophy (26,27), great care must be exercised to reproduce exactly the M-mode plane used to measure serial interventricular septal and left ventricular freewall dimensions. Echocardiographically derived left ventricular mass, dependent on symmetry of the ventricular dimensions, is not applicable in this disease process (28). In the future, three-dimensional left ventricular mass estimations (29) may offer the most reliable and accurate measure for patients with HOCM.

**Other HOCM treatment options.** Surgical myectomy or mitral valve replacement, or both, successfully relieves symptoms as well as decreases LVOT gradient (8,9,10, 11,13–15). Although operative mortality approximates 1%, surgical procedures have not yet been shown to alter the natural history of this disease process. A recent preliminary report (30) describes experience with nonsurgical myocardial reduction by selective catheterization of the first major septal artery followed by alcohol infusion to produce a localized infarct. For patients unresponsive to medications, or troublesome drug side effects, cardiac DCP may represent a reasonable option before an open cardiovascular surgical procedure.

**Pediatric pacing.** Permanent DCP is now the standard of care for many rhythm disturbances in children; pacing in HOCM is a novel application of this widely used therapy. Important developments in pacing technology include improved lead systems, smaller energy sources and multiprogrammable pulse generators (31). Pulse generators considered for the patient group should have rate-responsive features, variable AV delays with short AV interval options ($\leq$50 ms) and diagnostic counters.

**Cautions for pediatric HOCM pacing.** A recent editorial (32) sounded a cautionary note regarding DCP as a treatment strategy for patients with HOCM. Clearly, the ultimate role of DCP for patients with HOCM has yet to be completely defined. Certain considerations for pacing in pediatric patients may prove to be especially important. Smaller pediatric patients may still require epicardial pacemaker systems through either a sternotomy or thoracotomy. These smaller patients tend to have faster heart rates and shorter AV conduction intervals, which may make programming pacemaker variables more difficult. Congenital abnormalities of the mitral valve (23), although rare, can cause fixed intracavitary obstruction and prove to be unresponsive to pacing. Echocardiographic diagnosis of these mitral valve abnormalities before even temporary pacing should help direct these patients to more appropriate surgical mitral valve replacement.

**Summary.** For our study cohort, permanent DCP decreased LVOT gradient in selected (those responding to temporary DCP) pediatric patients with HOCM. This report represents our first evaluation of permanent pacing in pediatric patients with HOCM; our cohort was a limited patient series. A trial of temporary and ultimately permanent pacing may be worth considering as a treatment option in pediatric patients with HOCM who are unresponsive to medications. Symptoms unresponsive to long-term medications may likewise be dramatically improved in certain patients. Technical limitations still exist for application of this pacing technique in younger pediatric patients with HOCM. Ultimately the role of DCP for pediatric patients with HOCM may best be defined through collaborative, multicentered trials.

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