Ventricular Pacing With Premature Excitation for Treatment of Hypertensive-Cardiac Hypertrophy With Cavity-Obliteration

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Background—Hypertensive left ventricular hypertrophy with supranormal systolic ejection and distal cavity obliteration (HHCO) can result in debilitating exertional fatigue and dyspnea. Dual-chamber pacing with ventricular preactivation generates discordant contraction, which can limit cavity obliteration and thereby increase potential ejection reserve. Accordingly, we hypothesized that pacing may improve exercise tolerance long-term in this syndrome.

Methods and Results—Dual-chamber pacemakers were implanted in 9 patients with exertional dyspnea caused by HHCO. Intrinsic atrial rate was sensed, and ventricular preactivation was achieved by shortening the atrial-ventricular delay. Pacing was on or off for successive 3-month periods (randomized, double-blind, crossover design), followed by 6 additional pacing-on months. Metabolic exercise testing, quality-of-life assessment, and rest and dobutamine-stress echocardiographic/Doppler data were obtained. After 3 months of pacing-on, exercise duration rose from 324±133 to 588±238 s (mean±SD; P=0.001, with 7 of 9 patients improving ≥30%), and maximal oxygen consumption increased from 13.6±2.9 to 16.7±3.3 mL of O₂·min⁻¹·kg⁻¹ (P<0.02). Both parameters were little changed from baseline during the pacing-off period. Improved exercise capacity persisted at 1-year follow-up. Clinical symptoms and activities of daily living improved during the pacing-on period and stayed improved at 1 year, but they were little changed during the pacing-off period. Despite similar basal values, stroke volume (P<0.001) and cardiac output (P<0.02) increased with dobutamine stimulation 2 to 3 times more after 1 year of follow-up as compared with baseline.

Conclusions—Long-term dual-chamber pacing can improve exercise capacity, cardiac reserve, clinical symptoms, and activities of daily living in patients with HHCO. This therapy may provide a novel alternative for patients in whom traditional pharmacological treatment proves inadequate. (Circulation. 1999;100:807-812.)

Key Words: pacing ■ hypertension ■ exercise ■ hypotrophy ■ heart failure

Hypertension is a leading risk factor for the development of heart failure,1–3 particularly as age increases.2 As many as 30% to 40% of affected individuals have resting ejection fractions >50%, often with varying degrees of left ventricular (LV) hypertrophy.4–7 A subset of these patients develop severe hypertrophy with supranormal function and near-complete distal cavity obliteration during ejection.8 Such patients can experience profound exertional dyspnea and fatigue and intermittent pulmonary edema requiring hospitalization. Pharmacological therapy centers around β-receptor and calcium-channel blockers, diuretics, and angiotensin-converting enzyme inhibitors, yet many patients remain symptomatic, and alternative approaches are needed.

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Because heart failure symptoms occur in the absence of systolic abnormalities, the investigators focused on diastolic dysfunction to explain the pathophysiology of hypertensive hypertrophy with cavity obliteration.5,9 Another important factor, however, is the loss of systolic reserve. Once a heart ejects to very small cavity volumes at rest, it cannot reduce this volume further during stress demands, thereby limiting its reserve. Cardiac output can increase by the Frank-Starling mechanism, which risks diastolic pressure elevation in a hypertrophied heart, or by raising heart rate, which can compromise chamber filling time.10 Treatments that increase rest-end systolic volume, such as negatively inotropic β-receptor and calcium-channel blockers,11 may improve reserve, as volumes can again decline under stress.

Dual-chamber cardiac pacing with atrial sensing and premature ventricular activation (VDD mode) may provide a nonpharmacological alternative. Pacing generates discordant contraction and, thus, inhibits cavity obliteration by increasing end-systolic volume.12 To date, studies of pacing therapy in hypertrophied hearts have almost exclusively targeted patients with asymmetric septal thickening, systolic...
anterior motion of the mitral valve, and outflow tract obstruction. However, this specific pathophysiology is not required to observe functional effects from VDD pacing, as patients with symmetric hypertensive hypertrophy and distal cavity obliteration (HHCO) display very similar ventricular mechanical responses.

Accordingly, the present study was designed to test the hypothesis that long-term VDD pacing in patients with HHCO improves metabolic exercise performance and activities of daily living. As a secondary goal, we sought to determine potential mechanisms for such change, focusing on alterations in rest and adrenergic-stimulated cardiac reserve.

Methods

Patient Group

A total of 10 patients were recruited for the study over a period of 1.5 years. The sample size was set by Food and Drug Administration guidelines for a feasibility trial. One patient was diagnosed with primary hyperaldosteronism on the basis of data obtained shortly after pacemaker implantation and, therefore, was removed from the trial. Data from the 9 remaining patients are presented. All patients provided informed consent, and the study was approved by the Joint Committee on Clinical Investigation of the Johns Hopkins Medical Institutions.

All patients had documented exertional dyspnea (NYHA class III) despite hyperdynamic systolic function, with a mean estimated ejection fraction of 85.2 ± 7.1%. Three patients had been previously hospitalized for pulmonary edema. The mean age of the 4 male and 5 female patients was 58 ± 8 years. Four patients were black, and the others were white. All but one had well-documented histories of long-term, treated hypertension, spanning 18 ± 7 years, with mean systolic and diastolic arterial pressures of 157 ± 29.3 and 91.9 ± 15.9 mm Hg, respectively. The only patient without a documented hypertension history had not seen a physician for most of her adult life; however, she had a family history of hypertension and no history of familial hypertrophic disease.

All patients had concentric hypertrophy, with mean septal and LV free-wall thicknesses of 18.4 ± 2.5 and 16.3 ± 2.2 mm, respectively. None of the patients had significant mitral regurgitation or systolic anterior motion of the mitral valve. Mean outflow velocity assessed by continuous-wave Doppler was 244.2 ± 114 cm/s, which is consistent with an intracavitary pressure gradient of 28.5 ± 29.7 mm Hg. This gradient did not reflect outflow obstruction, but rather distal cavity obliteration and, thus, pressure differences between distal and basal LV regions. Figure 1 shows examples of echocardiogram images demonstrating marked hypertrophy with near-obliteration of the distal cavity at end-systole.

Long-term medications included calcium-channel blockers (verapamil or diltiazem 240 to 300 mg/d; n = 6), β-blockers (atenolol or metoprolol 12.5 to 75 mg/d; n = 5), angiotensin-converting enzyme inhibitors (captopril 10 to 40 mg/d; n = 3), and diuretics (n = 6).

Study Protocol

Baseline evaluation included metabolic exercise testing, ECG, rest and dobutamine-stimulated echo/Doppler studies, and the completion of a quality-of-life questionnaire (Minnesota Living with Heart Failure [MLHF]). Patients then received a permanent dual-chamber pacemaker (Thera-DR, Medtronic). The atrial lead was used to sense intrinsic sinus rhythm, and the right ventricular apical lead paced the heart. Premature ventricular activation was achieved by setting the
pacemaker atrial-ventricular delay shorter than the intrinsic PR interval (mean delay, 71 ms) (VDD mode). This delay was the longest possible that achieved full preexcitation at rest and during ambulation. Confirmation of capture during exercise was made during metabolic stress testing. At discharge, the pacemaker was either programmed on (VDD) or off (DDI, with low atrial backup rate); the choice of pacing mode was randomized and double-blinded. After 3 months, patients underwent repeat assessment, and pacing was then switched for the remaining 3 months. After follow-up evaluation, pacing resumed in all patients for an additional 6 months (total, 1 year), at which time final tests were performed. This final test included a repeat rest and dobutamine-stress echo/Doppler study.

Long-term medications were continued throughout the study, and medication adjustments by the patients’ primary care physicians were permitted. During the initial 6 months (blinded, crossover protocol), changes were made in only 2 patients; the diuretic dose was increased in both and the atenolol dose was increased (75 to 100 mg/day) in one. As these changes were made shortly after pacemaker implantation, they applied similarly during much of the protocol (specifically for on versus off comparisons). During the second 6-month period, the β-blocker dose was doubled in 2 additional patients, and captopril was converted to lisinopril in a third.

Testing Procedures

Metabolic testing was performed during maximal effort upright treadmill exercise with continuous ventilatory gas-exchange monitoring (MedGraphics). Exercise followed a Naughton protocol, with a fixed treadmill rate of 2.0 mph and incremental elevations of 3.5 degrees every 3 minutes. These data were used to obtain total exercise duration; the peak rate of oxygen consumption (maximal VO₂), reflecting the oxygen transport capacity of the circulatory system; and the VO₂ at the anaerobic threshold. The anaerobic threshold is the exercise level at which energy production from anaerobic metabolism becomes significant, and it is an endurance measure for exercise and activities of daily living. Lastly, peak exercise heart rate, systolic blood pressure, and the maximal rate-pressure product (RPPmax) were determined.

Echocardiographic and Doppler studies were performed at baseline and after 1 year to assess wall thickness, chamber diameter, fractional shortening, LV mass (area/length method), and LV outflow tract mean flow velocity, which was determined by continuous-wave Doppler. The latter provided an estimate of intracavitary pressure gradients associated with hyperdynamic contraction. Dobutamine stress-echocardiography was performed to assess cardiac reserve. Patients received intravenous dobutamine in incremental doses to maximal tolerated levels (7.5 to 40 μg · kg⁻¹ · min⁻¹). Dobutamine stress results were compared at a matched dose in all but 2 patients. One 1-year follow-up data were recorded only at the 40 μg · kg⁻¹ · min⁻¹ dose, versus the 30 and 20 μg · kg⁻¹ · min⁻¹ doses used at baseline in each, respectively. The average dose used for baseline and 1-year studies was 25 ± 12.8 versus 29 ± 13.6 μg · kg⁻¹ · min⁻¹, respectively (P = 0.2).

Chamber-diameter and wall-thickness measurements were made under rest conditions using commercial software. The ECG was not displayed on the echocardiographic monitor; therefore, analysis was blinded to pacing conditions (on versus off). All echocardiographic and flow gradient data were determined at the time of the procedure, and the technician was blinded to prior results. Baseline and dobutamine-stimulated stroke volume and cardiac output were determined from either aortic flow velocity × aortic root area or cavity volumes calculated from biplane images. These data were an average from at least 3 separate cycle determinations performed by a single observer blinded to data source.

Statistical Analysis

For the randomized, blinded portion of the study (baseline, pacing on, and pacing off), data were analyzed by repeated-measures analysis of variance (RMANOVA), with protocol period and patient number as fixed factors, and individual subjects as a random factor. Post-hoc testing of individual mean differences due to protocol period was performed using a Tukey test.

Results

VDD Pacing and Exercise Performance

Four patients were randomized to have pacing on during the first 3 months, and the remaining patients had active pacing during the second 3 months. Exercise capacity improved during the pacing-on period in nearly all patients. Figure 2 provides individual and summary data comparing exercise duration, maximal VO₂, and RPPmax at initial baseline to pacing-on and pacing-off periods. Randomization order is coded in the figure. With active pacing, total exercise duration lasted an average of 82% longer, from 324 ± 133 to 588 ± 239 s (P = 0.001 by RMANOVA with multiple comparisons test). Although there was heterogeneity in this response, 7 of 9 subjects experienced ≥30% improvement in exercise duration. Maximal VO₂ increased 24%: from 13.5 ± 2.9 to 16.7 ± 3.3 mL of O₂ · min⁻¹ · kg⁻¹ (P = 0.05), with all but 2 patients experiencing at least a 10% increase. VO₂ at the anaerobic threshold increased from 8.6 ± 0.97 to 11.4 ± 1.9 mL of O₂ · min⁻¹ · kg⁻¹ (P = 0.005). RPPmax rose 46%, from 15.6 ± 3.2 to 22.8 ± 3.3 mm Hg · beats/s · 10⁻⁵ (P = 0.002), indicating that prolonged exercise duration and maximal VO₂ were associated with enhanced total cardiac work. Resting RPP was similar for all periods.

Figure 2. Exercise capacity in patients with HHCO is enhanced by VDD-pacing therapy. Data are shown at baseline (BASE) and during 2 consecutive, randomized 3-month periods of pacing on (P-ON) or off (P-OFF). Individual data are displayed on left, and summary results to right. Randomization order of pacing-on first (Group A) or second (Group B) is denoted by solid lines/circles or dashed lines/open circles, respectively. Overall RMANOVA probability values are shown in parentheses to right, and results of multiple comparisons tests are over brackets. With VDD pacing, exercise duration, maximal VO₂, and peak exercise heart rate–systolic pressure product rose significantly. This was not observed when pacing was off. P = 0.01 for paired t-test of pacing on versus pacing off.

Data after 1 year were analyzed separately because the latter 6-month period was unblinded and the duration of contiguous pacing varied with initial randomization. For this comparison, data were assessed by a nonparametric Wilcoxon test. Data are presented as mean ± SD.
TABLE 1. Metabolic Exercise Results at 1-Year Follow-Up Compared With Baseline

<table>
<thead>
<tr>
<th>Exercise time, s</th>
<th>Baseline</th>
<th>1 Year</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rest VO₂, mL of O₂ · min⁻¹ · kg⁻¹</td>
<td>3.9±0.7</td>
<td>3.3±0.7</td>
<td>0.06</td>
</tr>
<tr>
<td>Max VO₂, mL of O₂ · min⁻¹ · kg⁻¹</td>
<td>13.6±2.9</td>
<td>14.7±4.5</td>
<td>NS</td>
</tr>
<tr>
<td>VO₂–AT, mL of O₂ · min⁻¹ · kg⁻¹</td>
<td>8.6±0.97</td>
<td>10.1±1.5</td>
<td>0.05</td>
</tr>
<tr>
<td>RPPₘₐₓ, mm Hg · beats/min · 10⁴</td>
<td>15.6±3.3</td>
<td>20.6±5.8</td>
<td>0.012</td>
</tr>
</tbody>
</table>

AT indicates anaerobic threshold.

None of these or any other exercise performance indexes were altered from baseline during the 3-month pacing-off period. All but one patient had a lower maximum VO₂ during pacing-off than pacing-on. Paired comparisons made solely between pacing-on versus pacing-off data revealed significant differences in exercise duration (P=0.024) and maximum VO₂ (P=0.01).

Improved exercise capacity was generally sustained at the 1-year follow-up (Table 1). Exercise duration and RPPₘₐₓ remained substantially increased over baseline (and pacing-off period) at 1 year. Maximal VO₂ was not significantly elevated; however, an 18% decline in resting VO₂ existed (P=0.007). In addition, VO₂ at the anaerobic threshold tended to increase (P=0.05). These results suggested an improvement in exertional efficiency. Initially, 8 of 9 patients developed dyspnea and 3 developed dizziness during exercise, which led to its termination. After 1 year of therapy, only 1 patient developed either symptom (P<0.001; χ² test), and the most common reason for stopping exercise was leg fatigue.

Pacing and Quality of Life Assessment

Figure 3 displays the total MLHF questionnaire scores during the initial controlled crossover portion of the study. The baseline MLHF score was 67.7±22.6 and it improved to 33.4±27.7 during the pacing-on period (P=0.008). In contrast, the score was 47.2±27.6 during the pacing-off period (P=0.18 versus baseline by RMANOVA). Symptomatic improvement was also generally sustained at 1 year (33.4±23.8; P=0.008). There was evidence of a substantial placebo effect, as MLHF score also declined considerably in the 5 patients who had pacing off during the initial 3 months.

![Figure 3](http://circ.ahajournals.org/)

Figure 3. Changes in total MLHF-questionnaire score for initial, randomized, double-blinded study periods. Significant improvement (decline) occurred in scores during pacing-on period; this was less marked during pacing-off period. Abbreviations and symbols are as in Figure 2.

TABLE 2. Resting Echocardiographic and Doppler Assessment at 1-Year Follow-Up Compared With Baseline

<table>
<thead>
<tr>
<th>Heart rate, min⁻¹</th>
<th>Baseline</th>
<th>1 Year</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>60.3±8.0</td>
<td>61.4±8.2</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>End-diastolic diameter, mm</td>
<td>44.1±5.9</td>
<td>47.3±6.7</td>
<td>0.04</td>
</tr>
<tr>
<td>Mean wall thickness, mm</td>
<td>17.9±3.3</td>
<td>15.9±2.3</td>
<td>0.03</td>
</tr>
<tr>
<td>Radius/thickness ratio</td>
<td>1.29±0.43</td>
<td>1.52±0.35</td>
<td>0.04</td>
</tr>
<tr>
<td>Estimated wall mass, g</td>
<td>273.3±84.3</td>
<td>257.2±84.7</td>
<td>0.015</td>
</tr>
<tr>
<td>Mean LV outflow velocity, cm/s</td>
<td>244.2±114</td>
<td>182.9±74</td>
<td>0.024</td>
</tr>
<tr>
<td>Estimated intracavitary pressure gradient, mm Hg</td>
<td>28.5±29.7</td>
<td>15.3±13.5</td>
<td>0.05</td>
</tr>
<tr>
<td>Fractional shortening, %</td>
<td>62.7±9.8</td>
<td>58.4±17.2</td>
<td>NS</td>
</tr>
<tr>
<td>E:A ratio</td>
<td>1.16±0.74</td>
<td>1.4±1.0</td>
<td>NS</td>
</tr>
<tr>
<td>E-wave deceleration time, ms</td>
<td>252±64</td>
<td>221±57.6</td>
<td>NS</td>
</tr>
<tr>
<td>Stroke volume, mL</td>
<td>82.5±24</td>
<td>82.5±21</td>
<td>NS</td>
</tr>
<tr>
<td>Cardiac output, L/min</td>
<td>5.0±1.8</td>
<td>5.1±1.2</td>
<td>NS</td>
</tr>
</tbody>
</table>

E:A ratio indicates early to late filling ratio.

(74.6 versus 42.6; P=0.057). However, unlike the pacing-on period, no corresponding changes in metabolic exercise data existed during the pacing-off period in these subjects.

Echocardiographic/Doppler Data

Table 2 provides baseline and 1-year follow-up echocardiographic/Doppler data. Resting chamber diameter at the papillary muscle level increased and average midwall thickness declined; thus, the radius/thickness ratio increased. These changes were modest but significant. A corresponding 6.4±5.7% decline in wall mass occurred (P<0.05). Resting stroke volume, cardiac output, and fractional shortening did not significantly change between baseline and 1-year follow-up. Similarly, diastolic function assessed by the early-to-late filling ratio and E-wave deceleration time was not significantly altered.

In contrast to rest function, cardiac reserve assessed during dobutamine stimulation was increased after 1 year of pacing therapy. Figure 4 displays absolute stroke volume and cardiac output at the 2 observation times: before and after receiving matched or nearly matched dobutamine doses. The 2 patients who received slightly higher doses at 1 year (see Methods) did not display the larger changes in either parameter. At baseline, LV stroke-volume change with dobutamine varied, and it was not significant overall (8.1±21 mL). In contrast, stroke volume rose by 30±24 mL (P=0.001) after 1 year (P=0.009 versus baseline response). The improvement in dobutamine response was not related to a change in resting stroke volume between the initial and final studies (P=0.84). Likewise, baseline cardiac output increased more with dobutamine after 1 year of pacing (+4.8±5.2 L/min; P=0.02) than it did during the initial study (+2.4±3.1 L/min, P=0.04; P=0.02 versus 1-year response). Further evidence that functional reserve was altered was found in the maximal tolerated dobutamine doses. Initially, only 3 patients tolerated a 40 μg · kg⁻¹ · min⁻¹ dose, with all 9 experiencing anginal-type chest pain and 6 developing dyspnea. In contrast, all patients tolerated the higher dose after 1 year of follow-up, with only 1 experiencing anginal-type pain and none developing dyspnea.
Discussion

This study demonstrates for the first time that long-term VDD pacing can improve exercise capacity, clinical symptoms, and the daily living activity of patients with severe exertional dyspnea and fatigue due to HHCO. In two-thirds of the patients, exercise duration increased substantially after 1 year (>50% in each; mean, 162%), and all but one improved at least 15%. The data further supports the hypothesis that VDD pacing increases systolic ejection reserve, and this may contribute to enhanced exercise capacity.

Study Limitations

This study was designed as a feasibility trial and was, therefore, limited in sample size. Although clearly a limitation, the randomized, blinded, crossover design enhanced the power of the study, enabling delineation of changes beyond those from a placebo effect. We also intentionally restricted the entry criteria to generate a fairly homogeneous population. Although mean changes were often large, not every patient benefited similarly, and some had only modest gains. Confirmation of the present results in a much larger cohort is needed, particularly to define which patients are mostly likely to benefit. Lastly, 4 patients had their β-blocker and/or diuretic dose increased between the initial and final studies, and some effect on the results cannot be ruled out. However, it could not have altered comparisons between randomized pacing on and off periods because the medication changes occurred either very early or after this period was completed. Furthermore, the 3 patients on higher β-blocker doses after 1 year displayed negligible differences in basal heart rate or cardiac output and did not have discernibly improved symptoms, exertional capacity, or dobutamine-stimulated reserve compared with other patients.

Mechanisms of Improved Functional Reserve

In a recent study of patients with HHCO or familial hypertrophic cardiomyopathy, apical pacing generated discoordinate wall motion at the pacing site, shifting the end-systolic pressure-volume relation rightward.12 The result was an increase in LV end-systolic volume at any given arterial or volume load, which exceeded that normally obtainable by these hearts in the absence of pacing. Sympathetic activation of the heart during stress decreases end-systolic volumes, shifting the end-systolic pressure-volume relation leftward. By increasing basal end-systolic volumes and not directly inhibiting sympathetic drive, VDD pacing may restore some of this reserve capacity.

Reduction of distal cavity compression may also improve mechanoenergetics, because once the distal chamber is at near-zero volume, subsequent systolic force contributes little to ejection but can increase cardiac internal work. Preventing cavity obliteration can reduce this wasted energy12 and might underlie reported declines in blood flow and flow heterogeneity.22 We could not directly demonstrate increased end-systolic volumes in our patients given the complex end-systolic geometry. However, end-diastolic dimension increased and stroke volume (derived by Doppler flow) remained unchanged, suggesting this increase occurred. Additional evidence was provided by the decline in mean outflow flow velocity, indicating reduced cavity obliteration. Lastly, exercise duration remained considerably prolonged at 1 year, despite little change in maximal VO₂. This is consistent with enhanced exercise efficiency that could reflect better conditioning, and/or more effective cardiovascular reserve.

The effects of VDD pacing on diastolic function remain unclear. We previously reported chamber compliance was unchanged by acute VDD pacing,12 but no data exist regarding long-term pacing. If anything, relaxation prolongs with discoordinate contraction from pacing23 and, given the role of diastolic dysfunction in hypertrophic disorders, this has raised concerns.17,24 Yet, we found VDD pacing improved exercise function and symptoms without a demonstrable benefit (or worsening) of diastolic function. This suggests that while diastolic abnormalities undoubtedly contribute to exercise intolerance in patients with HHCO, they are not the only factor. As noted, these patients also had limited systolic reserve capacity associated with basal hyperejection, and this may play a greater role in their symptoms.

Our study targeted patients with increased basal LV outflow velocity consistent with modest intracavitary pressure gradients from distal-wall compression. It is important to emphasize again that none of the patients had outflow obstruction. Rather, the velocities and estimated gradients reflected a small resting end-systolic volume that limited any further reduction with exercise. It remains possible, if not likely, that patients who only cavity-oblitereate during exercise would still benefit from VDD pacing. Lastly, the same pathophysiology occurs in elderly individuals with hypertrophic disease,8 many of whom have systolic hypertension. VDD pacing in individuals with refractory exertional dyspnea might also prove useful.

Comparison with Pacing Therapy for Familial Hypertrophic Cardiomyopathy

The usefulness of pacing to treat familial hypertrophic cardiomyopathy with asymmetric septal hypertrophy and intra-
ventricular cavity gradients has been the focus of several recent studies and reviews. The primary hypothesis is that by altering the ventricular activation sequence, pacing limits septal motion, reducing outflow gradients and improving symptoms. Initial, non-placebo-controlled studies suggested consistent success, whereas subsequent trials using controlled/crossover designs similar to that used in the present study have been less consistent. For example, Nishimura et al. reported only modest changes in exercise duration (414 versus 342 s), no change in maximal VO₂, and no clinical improvement in >30% of patients. Exercise capacity was also unchanged in the recent, larger Pacing in Hypertrophic Cardiomyopathy trial, although it rose 21% in those patients with <10 minutes of exercise time at baseline.

With this background, the current study is intriguing in that exercise capacity improved in most patients and generally was associated with objective improvement in metabolic and hemodynamic performance. Furthermore, reduced symptoms and enhanced exercise capacity were sustained with long-term treatment, which makes it less likely to reflect a placebo effect. The difference may lie in particular characteristics of the study population. In the present study, all patients had substantial baseline exertional disability, with an exercise duration <6 minutes and maximal VO₂<14 mL of O₂·kg⁻¹·min⁻¹, and none had outflow tract obstruction, mitral regurgitation, malignant arrhythmias, or cavity distortion caused by asymmetric disease. Echocardiograms in these individuals were generally similar, with symmetric hypertrophy and distal cavity obliteration. Ventricular pacing generates regional discoordinate motion at the pacing site, thereby limiting cavity compression. In patients with HHCO, the symmetry and more distal distribution of hypertrophy could, thereby, enhance the efficacy of apical pacing. In contrast, patients with proximal septal hypertrophy may depend more on a timing delay between an apical pacing stimulus and septal shortening, and such timing could vary considerably among patients.

Conclusions
Congestive failure is a leading cause of cardiovascular morbidity and mortality in older adults, yet nearly 40% of these individuals have preserved ejection fraction. In a subset of individuals with hypertensive, supranormal ejection and near-cavity obliteration, VDD pacing may offer a useful adjunct to pharmacological therapies. Further multicenter trials are needed to confirm the present findings and define the criteria for predicting patients most likely to benefit.

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References
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