Use of Doppler Echocardiography and Amyl Nitrite Inhalation to Characterize Left Ventricular Outflow Obstruction in Hypertrophic Cardiomyopathy*

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The presence of left ventricular outflow tract obstruction (LVOTO) of either a resting or dynamic nature may have important therapeutic and prognostic implications in patients with hypertrophic cardiomyopathy (HCM). Doppler echocardiograms combined with amyl nitrite (Amyl) inhalation were performed in 333 consecutive patients referred for suspected HCM to diagnose and categorize the nature and severity of LVOTO. Hypertrophic cardiomyopathy was present by 2-D and M-mode criteria in 145/333 (44 percent) patients. Normal limits of resting and post-Amyl continuous wave Doppler peak left ventricular outflow tract velocities were established in 15 subjects with completely normal 2-D and Doppler echocardiograms. Based on these criteria, of the 145 patients with HCM, 63 (43 percent) were classified as having resting LVOTO, peak velocity 4.2±1.3 m/s. Among 82 patients with HCM without resting LVOTO, 47 (57 percent) received Amyl. Latent LVOTO was provoked in 25/47 (53 percent), peak post-Amyl velocity 4.5±1.2 m/s. The remaining 22 (47 percent) had nonobstructive HCM, as indicated by no significant increase in post-Amyl velocity. Among a total 62 subjects receiving Amyl, none experienced serious morbidity or mortality. Doppler echocardiography, in conjunction with Amyl inhalation in selected patients, is a useful noninvasive method to diagnose and categorize patients with HCM according to the nature and severity of LVOTO.

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Patients with hypertrophic cardiomyopathy (HCM) may be categorized according to the presence and severity of left ventricular outflow tract obstruction (LVOTO). Such a classification identifies three hemodynamic subsets: absence of LVOTO, resting LVOTO, and latent or provokable LVOTO, all of which may have different therapeutic and prognostic significance.1-10 Continuous wave Doppler combined with 2-D and M-mode echocardiography offers a useful means by which to identify these hemodynamic subsets. Although inhalation of the vasodilator, amyl nitrite (Amyl), has long been recognized as a means to provoke latent LVOTO in patients with HCM, the value and safety of Amyl in patients undergoing ambulatory Doppler echocardiography has not been studied in a systematic fashion. The purpose of this study was to characterize the nature and severity of LVOTO in a consecutive series of patients referred for evaluation of clinically suspected HCM using Doppler echocardiography, and in selected instances, in combination with Amyl inhalation.

Methods

Patient Population

All patients referred for Doppler echocardiographic evaluation of clinically suspected HCM during the period between January 1985 and June 1988 were enrolled. Baseline data, which were collected on 333 consecutive patients, included age, sex, and the reason for referral. Doppler echocardiograms were performed without changes in medications.

Echo-Doppler Evaluation

Echocardiograms were obtained using commercially available ultrasound units fitted with either 2.5-, 3.5-, or 5.0-MHz transducers. All patients had complete M-mode, 2-D, and pulsed wave Doppler studies from standard approaches. Continuous wave Doppler interrogation of the left ventricular outflow tract was performed in all patients using a 1.9-MHz nonimaging transducer. The transducer was positioned at the left ventricular apex and direction, wall filter, and gain settings were adjusted to optimally display the left ventricular outflow tract Doppler signal. Care was taken to exclude signals of mitral valve insufficiency that might mimic the outflow tract signal.

Doppler echocardiograms were recorded on high-fidelity video tape and analyzed off-line using a commercially available computer, software, and digitizing pad (Nova Microsonics, Inc, Mahwah, NJ). Left ventricular chamber and wall thickness measurements were made from the parasternal M-mode tracing, according to recommendations of the American Society of Echocardiography.11 The presence of systolic anterior motion of the mitral valve apparatus was noted if present in any 2-D or M-mode view. The severity of mitral systolic anterior motion was assessed by measurement of the septal-mitral valve distance at the onset of systole.9 The Doppler left ventricular outflow waveform was assessed for its contour and peak velocity.

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Amyl Nitrite Challenge

Amyl inhalation was routinely used when (1) anatomic criteria for HCM were fulfilled in the absence of resting Doppler LVOTO, or (2) there were no anatomic findings of HCM but the referring physician had specifically requested Amyl challenge, regardless of echocardiographic findings. Amyl inhalation was not performed when (1) anatomic criteria for HCM were present but resting Doppler LVOTO was noted (n = 63); (2) anatomic criteria for HCM were present but the patient was taking β-blockers and had a resting heart rate below 50 beats per minute (n = 4); (3) anatomic criteria for HCM were present but contraindications to Amyl were noted (recent stroke, unstable angina pectoris, aortic stenosis, pregnancy, previous hypersensitivity to nitrates) (n = 31); or (4) no anatomic findings of HCM were detected (n = 173).

Amyl nitrite (Vaporole, Burroughs Wellcome Co, Research Triangle Park, NC) was administered after crushing a 0.3-ml glass capsule. The subject was instructed to take five to six deep inhalations from the capsule held at the nares while he or she was in a modified left lateral decubitus position. Inhalations were performed under the direct supervision of a physician. Patients were monitored during inhalation challenges with a single-channel electrocardiogram and they were frequently questioned regarding potential adverse reactions. Continuous wave Doppler examinations of the left ventricular outflow tract from the apical position were performed immediately prior to and for three to five minutes continuously after Amyl inhalation.

Definitions

Echocardiographic criteria for the anatomic diagnosis of HCM were as follows: (1) asymmetric septal hypertrophy with an end-diastolic septal wall thickness (SWT) greater than 1.3 cm and a ratio of SWT to posterior wall thickness (PWT) greater than 1.3:1, or (2) concentric left ventricular hypertrophy with an end-diastolic SWT and PWT greater than 1.3 cm, and (3) either normal or hyperdynamic systolic left ventricular function by visual estimate.12 Patients were excluded if aortic valve thickness, diminished cusp mobility, membranous subvalvular stenosis, supravalvular aortic stenosis, or left ventricular hypoperistalsis were noted by echocardiography, or if chronic renal failure or other clinical conditions, other than mild essential hypertension, which might cause left ventricular hypertrophy were present.

The normal ranges for continuous wave Doppler peak left ventricular outflow velocities both at rest and following Amyl were identified from the 2 SD limits obtained in 15 patients who received Amyl at the request of their referring physician despite normal 2-D, M-mode, and Doppler echocardiograms. Based on these criteria, resting LVOTO was defined as a peak Doppler velocity of more than 2.1 m/s, with echocardiographic evidence of HCM. Latent LVOTO was defined as a normal resting Doppler velocity that increased to more than 2.7 m/s after inhalation of Amyl, with echocardiographic evidence of HCM. To ensure that the Doppler signal was due to LVOTO, only Doppler waveforms with characteristic late peaking velocities and without characteristics of mitral insufficiency were used (Fig 1). Absence of LVOTO was defined as a normal resting and post-Amyl peak Doppler velocity in association with echocardiographic evidence of HCM.

Table 1—Baseline Characteristics of Patient Subsets*

<table>
<thead>
<tr>
<th>Group</th>
<th>Age, yr</th>
<th>M:F</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertrophic cardiomyopathy</td>
<td>58.4 ± 15.8</td>
<td>53:92†</td>
</tr>
<tr>
<td>Resting obstruction</td>
<td>57.0 ± 16.3</td>
<td>21:42</td>
</tr>
<tr>
<td>(n = 63)</td>
<td>(8-86)</td>
<td></td>
</tr>
<tr>
<td>Latent obstruction</td>
<td>58.6 ± 17.6</td>
<td>11:14</td>
</tr>
<tr>
<td>(n = 25)</td>
<td>(14-84)</td>
<td></td>
</tr>
<tr>
<td>No obstruction</td>
<td>57.6 ± 14.5</td>
<td>3:19</td>
</tr>
<tr>
<td>(n = 22)</td>
<td>(17-78)</td>
<td></td>
</tr>
<tr>
<td>Amyl not given</td>
<td>61.1 ± 16.5</td>
<td>18:17</td>
</tr>
<tr>
<td>(n = 35)</td>
<td>(15-82)</td>
<td></td>
</tr>
<tr>
<td>No hypertrophic cardiomyopathy</td>
<td>59.0 ± 14.4</td>
<td>104:84</td>
</tr>
<tr>
<td>Normal subjects, Amyl given</td>
<td>63.6 ± 12.2</td>
<td>7:8</td>
</tr>
<tr>
<td>(n = 15)</td>
<td>(16-83)</td>
<td></td>
</tr>
<tr>
<td>Normal subjects, no Amyl given</td>
<td>58.4 ± 13.6</td>
<td>48:35</td>
</tr>
<tr>
<td>(n = 83)</td>
<td>(1-78)</td>
<td></td>
</tr>
<tr>
<td>Other cardiovascular diseases</td>
<td>58.2 ± 16.6</td>
<td>49:41</td>
</tr>
<tr>
<td>(n = 90)</td>
<td>(8-86)</td>
<td></td>
</tr>
</tbody>
</table>

*M = male; F = female; and Amyl = amyl nitrite inhalation. Age values are mean ± 1 SD. Values in parentheses represent entire range of observed values.

†χ² comparison of sex distribution; hypertrophic cardiomyopathy group vs no hypertrophic cardiomyopathy group, χ² = 11.6, p < .05.
Table 2—Echo-Doppler Parameters in Normal Subjects Receiving Amyl Nitrite*

<table>
<thead>
<tr>
<th>Subject No./Age, yr</th>
<th>LVIDd, cm</th>
<th>PWTd, cm</th>
<th>SWTd, cm</th>
<th>Doppler Peak Resting Velocity, m/s</th>
<th>Doppler Peak Velocity Following Amyl, m/s</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/47</td>
<td>4.5</td>
<td>0.9</td>
<td>1.0</td>
<td>1.4</td>
<td>2.0</td>
</tr>
<tr>
<td>2/60</td>
<td>4.5</td>
<td>1.1</td>
<td>1.1</td>
<td>1.7</td>
<td>2.1</td>
</tr>
<tr>
<td>3/65</td>
<td>4.1</td>
<td>0.8</td>
<td>0.9</td>
<td>0.9</td>
<td>2.0</td>
</tr>
<tr>
<td>4/42</td>
<td>4.4</td>
<td>1.0</td>
<td>1.1</td>
<td>1.8</td>
<td>2.3</td>
</tr>
<tr>
<td>5/61</td>
<td>4.6</td>
<td>0.9</td>
<td>1.0</td>
<td>1.2</td>
<td>1.7</td>
</tr>
<tr>
<td>6/6</td>
<td>3.0</td>
<td>0.5</td>
<td>0.8</td>
<td>1.0</td>
<td>1.8</td>
</tr>
<tr>
<td>9/73</td>
<td>4.7</td>
<td>0.7</td>
<td>1.0</td>
<td>1.9</td>
<td>2.5</td>
</tr>
<tr>
<td>8/68</td>
<td>4.0</td>
<td>1.2</td>
<td>1.1</td>
<td>2.0</td>
<td>2.4</td>
</tr>
<tr>
<td>9/69</td>
<td>4.2</td>
<td>1.2</td>
<td>1.2</td>
<td>1.8</td>
<td>2.6</td>
</tr>
<tr>
<td>10/66</td>
<td>4.3</td>
<td>0.9</td>
<td>1.1</td>
<td>1.5</td>
<td>2.5</td>
</tr>
<tr>
<td>11/48</td>
<td>4.1</td>
<td>0.8</td>
<td>0.9</td>
<td>1.5</td>
<td>1.8</td>
</tr>
<tr>
<td>12/61</td>
<td>4.8</td>
<td>1.0</td>
<td>1.2</td>
<td>1.3</td>
<td>2.2</td>
</tr>
<tr>
<td>13/55</td>
<td>4.3</td>
<td>1.1</td>
<td>1.0</td>
<td>1.6</td>
<td>2.0</td>
</tr>
<tr>
<td>14/83</td>
<td>4.6</td>
<td>1.2</td>
<td>1.1</td>
<td>1.4</td>
<td>1.8</td>
</tr>
<tr>
<td>15/60</td>
<td>4.1</td>
<td>0.9</td>
<td>1.1</td>
<td>1.3</td>
<td>1.7</td>
</tr>
<tr>
<td>Mean ± 1 SD/63.6 ± 12.2</td>
<td>4.3 ± 0.4</td>
<td>0.9 ± 0.2</td>
<td>1.0 ± 0.1</td>
<td>1.5 ± 0.3</td>
<td>2.1 ± 0.3</td>
</tr>
</tbody>
</table>

2 SD upper limit
>2.1
>2.7

*LVIDd = left ventricular internal dimension (end-diastole); PWTd = posterior wall thickness (end-diastole); SWTd = septal wall thickness (end-diastole); and Amyl = amyl nitrite inhalation. Velocities represent continuous wave Doppler peak left ventricular outflow tract velocities in meters per second.

Statistics

Results were expressed as mean ± 1 SD. Comparisons between groups for continuous variables were performed using Student's t tests for unpaired samples. For categoric variables, comparisons were by χ² analysis. A p value < .05 was considered statistically significant.

RESULTS

Baseline characteristics of all patient groups are indicated in Table 1. No differences in age were detected among the patient groups. More women than men were noted in the group with HCM than the group without HCM.

Echocardiographic and Doppler parameters in the 15 normal subjects who underwent Amyl inhalation are shown in Table 2. No normal subject had resting systolic anterior movement of the mitral valve. Using 2 SD limits, normal Doppler peak resting left ventricular outflow tract velocity was established as ≤2.1 m/s. The normal peak left ventricular outflow tract velocity after Amyl was established was ≤2.7 m/s.

Based on these Doppler criteria and the echocardiographic criteria previously set forth, patients were categorized as shown in Figure 2. Of 333 patients referred for suspected HCM, 145 (44 percent) had their conditions positively diagnosed by echocardiographic criteria. Of these, 63 (45 percent) had resting LVOTO. Of the 92 patients without resting LVOTO, 47 (57 percent) received Amyl inhalation. Latent LVOTO was provoked in 25 (53 percent) and was absent in 22 (47 percent). The 188 patients who did not meet criteria for a diagnosis of HCM had their conditions diagnosed as follows: normal, 98 (52 percent); aortic valve disease, 35 (19 percent); left ventricular hypertrophy of another cause, 24 (13 percent); and other cardiovascular diseases (eg, mitral valve prolapse), 31 (16 percent).

Echocardiographic and Doppler values obtained in each of the Doppler-defined hemodynamic subsets of patients with HCM are shown in Table 3. These indicate that patients with resting LVOTO, by definition, had significantly higher Doppler peak outflow tract velocities, with a greater frequency and severity of systolic anterior movement of the mitral valve, greater septal and posterior wall hypertrophy, and a smaller ventricular chamber dimension than the other groups. Patients with 2-D evidence of HCM and latent LVOTO had greater septal wall hypertrophy, but less posterior wall hypertrophy, and a greater frequency and severity of systolic anterior movement of the mitral valve apparatus at rest than patients with HCM.
Table 3—Echo-Doppler Parameters in Patients with Hypertrophic Cardiomyopathy

<table>
<thead>
<tr>
<th>Group</th>
<th>LVIDd, cm</th>
<th>PWTd, cm</th>
<th>SWTd, cm</th>
<th>Resting SAM, No. of Patients</th>
<th>S-MV Dist, cm</th>
<th>Doppler Peak Systolic Velocity, m/s</th>
<th>Doppler Peak Velocity Following Amyl, m/s</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resting obstruction</td>
<td>2.9±0.5†</td>
<td>1.8±0.5†</td>
<td>2.4±0.32†</td>
<td>61†</td>
<td>1.9±0.6†</td>
<td>4.2±1.3†</td>
<td>. . .</td>
</tr>
<tr>
<td>(n=63)</td>
<td>(1.7-3.6)</td>
<td>(1.3-2.6)</td>
<td>(1.4-3.0)</td>
<td></td>
<td>(0.9-3.2)</td>
<td>(2.2-8.0)</td>
<td>. . .</td>
</tr>
<tr>
<td>Latent obstruction</td>
<td>3.7±0.7‡</td>
<td>1.3±0.3‡</td>
<td>2.0±0.2‡</td>
<td>13‡</td>
<td>2.3±0.6‡</td>
<td>1.8±0.2</td>
<td>4.5±1.2‡</td>
</tr>
<tr>
<td>(n=25)</td>
<td>(1.9-4.6)</td>
<td>(1.0-1.8)</td>
<td>(1.4-2.3)</td>
<td></td>
<td>(1.4-3.3)</td>
<td>(1.4-5.1)</td>
<td>(2.9-7.0)</td>
</tr>
<tr>
<td>No obstruction</td>
<td>3.9±0.6</td>
<td>1.6±0.3</td>
<td>1.8±0.3</td>
<td>4</td>
<td>2.7±0.7</td>
<td>1.7±0.3</td>
<td>2.2±0.3</td>
</tr>
<tr>
<td>(n=32)</td>
<td>(2.1-4.9)</td>
<td>(1.1-2.1)</td>
<td>(1.4-2.4)</td>
<td></td>
<td>(1.8-4.3)</td>
<td>(1.1-2.0)</td>
<td>(1.5-2.6)</td>
</tr>
<tr>
<td>Amyl not given</td>
<td>3.9±0.6</td>
<td>1.5±0.4</td>
<td>1.8±0.3</td>
<td>12</td>
<td>2.8±0.5</td>
<td>1.8±0.4</td>
<td>. . .</td>
</tr>
<tr>
<td>(n=35)</td>
<td>(2.1-5.2)</td>
<td>(1.1-2.1)</td>
<td>(1.4-2.3)</td>
<td></td>
<td>(2.0-4.3)</td>
<td>(1.2-2.1)</td>
<td>. . .</td>
</tr>
</tbody>
</table>

*Abbreviations as in Table 2. Resting SAM = mitral valve systolic anterior movement at rest. S-MV Dist = septal-mitral leaflet distance at the onset of systole. Values given are mean ± 1 SD. Values in parentheses represent entire range of observed values.

†p<.05 for resting obstruction group vs all other groups.
‡p<.05 for latent obstruction group vs no obstruction group.

and no LVOTO. Notably, the resting left ventricular outflow velocities in normal subjects (Table 2) were equivalent to those in patients with HCM and latent LVOTO as well as those without LVOTO. Likewise, the post-Amy velocities in normal subjects were identical to the post-Amy velocities in patients with HCM without LVOTO.

Mild and transient headaches, nausea, and dizziness were frequently reported as side effects following Amy. No patient experienced syncope, either atrial or ventricular arrhythmias, or mortality associated with Amyl inhalation.

Discussion

Importance of Hemodynamic Subsets

Classification of patients with HCM according to the nature and severity of LVOTO may have important therapeutic and prognostic implications. Patients with resting LVOTO manifest the most severe and frequent symptoms as well as the most profound hemodynamic systolic and diastolic abnormalities.1-3,8,14,15 Untreated, this subset of patients has a poor prognosis, with one study reporting more than 50 percent to worsen symptomatically and 11 percent dying by four-year follow-up.10 For these reasons, aggressive therapy with β-blockers, calcium antagonists, negative inotropic agents, and a lower threshold to performing septal myomectomy has been advised in this group of patients.1,6,10 Patients with nonobstructive HCM tend to have fewer symptoms, yet they may still demonstrate significant hemodynamic abnormalities related to the extent of left ventricular hypertrophy.1-3,8,9,14,15 Calcium antagonist therapy, which has primarily been advised in this group of patients, may provide symptomatic and hemodynamic improvement as well as result in regression of left ventricular hypertrophy.1,6,10,17 Patients with latent LVOTO are usually the least symptomatic, with fewer atrial and ventricular arrhythmias, normal left ventricular end-diastolic pressures, and normal diastolic filling characteristics.1,3,4 Thus, β-blockers are considered agents of choice in treating this hemodynamic subset. Negative inotropic agents are believed to be contraindicated.4,6,7

ECHOCARDIOGRAPHIC CHARACTERISTICS OF SUBSETS

Although this study made no attempt to reproduce the clinical, hemodynamic, or prognostic distinctions previously noted and summarized above, the echocardiographic characteristics of the hemodynamic subsets noted in this study were similar to those previously described.1-3,5 Notably, patients with HCM with resting LVOTO had the greatest amount of both septal and posterior wall hypertrophy and the greatest frequency and severity of systolic anterior movement of the mitral valve. Patients with latent LVOTO had less posterior wall hypertrophy than either those with resting LVOTO or those without LVOTO. Septal wall thickness, however, was increased in patients with latent LVOTO in comparison to patients without LVOTO. The frequency and severity of systolic anterior movement of the mitral valve in patients with latent LVOTO was intermediate to patients with resting LVOTO and those without LVOTO.

Significance of Outflow Tract Gradients

Not only is the classification of patients according to the nature of LVOTO important, but so is an estimate of the severity of LVOTO. Although the controversy regarding the true pathologic significance of LVOTO persists, both “obstructionists” and “nonobstructionists” agree that elevated left ventricular pressures are detrimental to the left ventricle.12,18-20 There is good evidence to indicate that the degree of LVOTO relates to symptomatic status, and that improvement in symptoms resulting from either medical or surgical therapy is associated with concomitant decreases in the severity of LVOTO.1,15,19-22

Although to our knowledge no previous study has
characterized the distribution of hemodynamic subsets of patients with HCM using Doppler echocardiography, the data presented in this study are consistent with hemodynamic subsets identified previously by both clinical and invasive means. In a study by Rakowski et al, among 100 patients characterized clinically and hemodynamically by the nature of LVOTO, the distribution was such that 39 had resting LVOTO, 34 had latent LVOTO, and 27 had no obstruction. Similarly, in 70 patients who were hemodynamically characterized by left ventricular manometry and transseptal left atrial catheterization, 39 percent had resting LVOTO, 40 percent had latent LVOTO, and 21 percent had no obstruction. In the current series we noted 43 percent with resting LVOTO, 30 percent with latent LVOTO, and 27 percent with no obstruction. Importantly, with the use of combined Doppler and echocardiographic techniques, the diagnosis of HCM can be established entirely by noninvasive means. This not only overcomes potential complications related to cardiac catheterization and transseptal puncture, but also is not complicated by concerns of artificial gradients detected due to catheter entrapment.

Amyl Nitrite and Latent Obstruction

A variety of pharmacologic and physiologic maneuvers may be employed to provoke latent LVOTO. Among those commonly used are the Valsalva maneuver, ventricular extrasystoles, and administration of sympathomimetic agents and Amyl. While induction of extrasystoles and administration of sympathomimetics can be performed in the catheterization laboratory, they cannot be conveniently or safely used during routine echocardiography. The Valsalva maneuver, because it is difficult to perform, is frequently performed incorrectly and often results in loss of the Doppler signal due to chest wall movement; it has limited applicability in the evaluation of latent LVOTO. Amyl can be conveniently stored and administered. It has a rapid onset and offset of action, and during inhalation, continuous Doppler monitoring is possible so as to immediately detect any velocity changes.

This study provides important information regarding normal values for left ventricular outflow tract velocities at rest and following inhalation of Amyl. The results for normal aortic outflow velocity are consistent with ranges reported by previous investigators. Amyl is a potent peripheral and coronary vasodilator that also acts to decrease venous return, resulting in a reflex tachycardia and a secondary inotropic response. By virtue of the inotropic, chronotropic, and vasodilatory effects of Amyl, an increase in cardiac output is observed. Previous studies in normal subjects indicate that while much of the increase in cardiac output is due to an increased heart rate, small increases in stroke volume also occur. This in addition to a decrease in left ventricular outflow dimension may account for the small but consistent increase in Doppler peak left ventricular outflow velocity following Amyl inhalation in normal subjects. Thus, a physiologically normal increase in Doppler velocity must be taken into account when identifying patients with provoked LVOTO.

Relationship of Doppler Velocity to Gradient

The Doppler peak left ventricular outflow tract velocity relates to the pressure gradient at the site of obstruction. If the Doppler signal is obtained nearly parallel to the flow of blood, this relationship is described by the modified Bernoulli equation:

$$PG = 4(V)^2,$$

where $PG$ is the maximum instantaneous pressure gradient at the site of obstruction and $V$ is the peak Doppler velocity. There is experimental and clinical evidence to support a good relationship of the Doppler-derived peak gradient with that measured at manometry both at rest and following interventions in patients with HCM.

The mean \(\pm 1\) SD for peak left ventricular outflow velocity in patients with resting LVOTO was 4.2 \(\pm\) 1.3 m/s, with a peak velocity of 8.0 m/s measured in one patient. By the modified Bernoulli equation, these would correspond to a mean value for peak instantaneous gradient of 71 mm Hg and a maximally recorded peak instantaneous gradient of 256 mm Hg. Previous investigators have also noted that patients with HCM may demonstrate unusually high left ventricular outflow tract velocities and gradients. Additionally, Doppler left ventricular outflow tract signals demonstrated characteristic late systolic peaking, indicative of the development of the maximal gradient in mid to late systole. Analogous to patients with resting LVOTO, patients with latent LVOTO provoked by Amyl also developed unusually high peak left ventricular outflow velocities, late systolic peaking of Doppler waveforms, and elevations in peak instantaneous gradients to levels previously reported.

Precautions and Limitations

Differentiating the left ventricular outflow tract velocity from the Doppler signal of mitral insufficiency may be difficult. They may both show late peaking and unusually high velocities. In such cases, imaging-directed continuous wave imaging may be useful. Identification of mitral insufficiency by pulsed wave or color flow methods may also be of value. However, there is no substitute for experience in properly locating and identifying Doppler velocities assessed by continuous wave Doppler methods.

Another consideration is the well-known lability of
gradients in patients with HCM. Gradients have been reported to vary not only day to day, but also during the course of a cardiac catheterization.\textsuperscript{1,20,23,34} We made no attempt to reproduce the Amyl-induced gradients, but we would expect that the same lability noted by previous investigators would exist in this group of patients. Furthermore, no attempts were made to alter medications in use at the time of echo-Doppler studies. Nevertheless, the lability of the gradient does not appear to detract from the therapeutic and prognostic significance of identifying patients as having latent LVOTO.\textsuperscript{1,7}

Patients with HCM included in this study had either asymmetric septal or concentric left ventricular hypertrophy. While this accounts for 95 percent of patients with HCM, the findings herein are not applicable to the small subset of patients with midventricular, apical, or posteroseptal and/or lateral wall hypertrophy.\textsuperscript{1}

Of note is that patients whose cases were reported in this study were older than those whose cases were previously reported.\textsuperscript{19} This may be a result of including patients who were more symptomatic at the time of referral for Doppler echocardiographic evaluation, in which case an older age group would be expected.\textsuperscript{19} The increased female predominance would also be accounted for by this, as older patients with HCM tend to have an unusually high female proportion.\textsuperscript{19} Another explanation, however, for the older age group and female proportion would be inclusion of patients with the recently described syndrome of hypertensive cardiomyopathy of the elderly. These patients have been characterized as being elderly, mostly female, and having long-standing hypertension.\textsuperscript{41,42} Recently, such patients have also been characterized as having elevated left ventricular outflow tract velocities and similar Doppler waveforms as patients with classic HCM.\textsuperscript{42} Based on their described pathophysiologic features, it has been recommended that such patients also be treated in a manner similar to patients with classic HCM.\textsuperscript{41,42}

Although we encountered no serious complications in patients receiving Amyl inhalation, all inhalations were performed under the direct supervision of a physician and with continuous electrocardiographic monitoring. Importantly, of 82 patients eligible to receive Amyl, 31 (37 percent) were excluded because of contraindications or recent use of β-blockers. Because of the potential for serious side effects, the decision to administer Amyl should be made in concert with the patient's attending physician, who may be the only person with complete knowledge of the patient's clinical condition.

**Conclusions**

The results of this study confirm previous studies in identifying echocardiographic characteristics of hemodynamic subsets of patients with HCM. Importantly, the additional use of Doppler evaluation, combined with inhalation of amyl nitrite in selected patients, permits an entirely noninvasive characterization of the nature and severity of left ventricular outflow obstruction. Information obtained in this manner may then be used to assist in the treatment and prognostic assessment of patients with HCM.

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