Increased Intensity of the Murmur of Hypertrophic Obstructive Cardiomyopathy with Carotid Sinus Pressure*

Herman O. Klein, M.D.; Elio DiSegni, M.D.; Hadassa Dean, M.D.; Bruno Beker, M.D.; Aetnoam Bakst, M.B.; and Elieser Kaplinsky, M.D.

In a prospective study murmurs increased in intensity with carotid sinus pressure in 18 of 26 patients with hypertrophic obstructive cardiomyopathy (HOCM) (sensitivity, 69.2 percent for the 26 patients, 85.7 percent for the 21 patients in whom heart rate and blood pressure decreased with carotid sinus pressure). On the other hand, the murmur remained constant or decreased in all but one of 104 patients with valvular aortic stenosis, mitral insufficiency, hypertrophic nonobstructive cardiomyopathy, and systolic murmurs of miscellaneous origins (specificity, 99 percent; positive predictive value, 94.7 percent). Catheterization, indirect arterial pressure tracings, and echocardiographic studies indicated that carotid sinus pressure-induced bradycardia was associated with increased left ventricular outflow tract obstruction. The carotid sinus pressure-induced increase in the murmur is probably multifactorial: decreased aortic pressure and impedance; increased contractility immediately on sudden slowing of heart rate; further increase in obstruction as the mitral valve systolic anterior movement is enhanced; and delayed vasodilatation maintaining the obstruction even after return of heart rate to precataroid sinus pressure values. An increase in a systolic murmur with carotid sinus pressure is characteristic of HOCM.

Obstruction to left ventricular outflow is fixed in organic lesions of the outflow tract, e.g., valvular aortic stenosis. In contrast, the obstruction in hypertrophic cardiomyopathy (HOCM) is dynamic: its severity often changes dramatically with maneuvers that affect the autonomic nervous system and preload and afterload conditions and thus induce, pari passu, changes in left ventricular dimensions, pressure, and contractility.1

Clinically, the different effects of such interventions on the degree of obstruction have been used to differentiate at the bedside between HOCM and other types of left ventricular outflow tract obstruction. The murmur often changes quickly and quite dramatically in the former, while that of organic obstruction varies little with these interventions.1,6

The present prospective study describes the contrasting effects of carotid sinus pressure (CSP) on the murmur intensity of HOCM and other murmurs. The results suggest that a significant increase in a systolic murmur produced by CSP points to the probable existence of HOCM.

METHODS

A total of 130 patients with systolic murmurs of diverse origins were subjected to CSP. Changes in murmur intensity were carefully evaluated simultaneously with the changes in heart rate and blood pressure. The usual classification of murmur intensity was used to grade changes detected on auscultation.7 Absence or presence of thrills was arbitrarily ignored. Phonocardiography and carotid and brachial pulse tracings were recorded with a commercially available recorder (Smith and Kline Instrument Ekoline 21 and Hewlett-Packard Contact Sensors 21000A/B designed to detect heart sounds and pulse wave signals). Change or lack of change of murmur intensity was thus confirmed by visual inspection of the recording obtained during CSP. All patients were auscultated by at least one senior cardiologist (H.O.K.), and those patients in whom significant changes were noted were also independently evaluated by another senior cardiologist. Consensus opinion was obtained in each case for grading the murmurs and changes in intensity. Carotid sinus stimulation was performed by applying gentle digital pressure on the right carotid sinus. Both carotid arteries were previously inspected for patency and bruits. Pressure was gradually increased if heart rate failed to slow with initially gentle stimulation and was released as soon as heart rate slowed. Digital pressure was then similarly applied to the left carotid sinus if right CSP had had no effect. No complications were seen from CSP in this series.

Documentation of HOCM was based on the presence of systolic anterior movement of the mitral valve, asymmetric septal hypertrophy, and the typical bifid carotid pulse at rest, in postextrasystolic beats, or after amyl nitrite administration in all patients. Hypertrophic nonobstructive cardiomyopathy was diagnosed when systolic anterior movement of the mitral valve and mid systolic closure of the aortic valve were absent and the carotid pulse contour remained normal even after provocative maneuvers such as the Valsalva maneuver and amyl nitrite administration.

The sensitivity, specificity, and positive predictive value of a distinct increase in murmur intensity with CSP were calculated as follows:

\[
\text{sensitivity} = \frac{\text{true positives}}{\text{true positives} + \text{false negatives}} \times 100
\]

\[
\text{specificity} = \frac{\text{true negatives}}{\text{true negatives} + \text{false positives}} \times 100
\]

\[
\text{positive predictive accuracy of test (probability of HOCM if the murmur increases in intensity)} = \frac{\text{true positives}}{\text{true positives} + \text{false positives}} \times 100
\]

*From the Department of Cardiology, Meir General Hospital, Sapir Medical Center, Kfar Saba, and the Sackler School of Medicine, Tel-Aviv University, Israel.


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Reprint requests: Dr Klein, Cardiology Department, Meir General Hospital, Kfar Saba, Israel

Murmur of Hypertrophic Obstructive Cardiomyopathy (Klein et al)
**RESULTS**

**Hypertrophic Obstructive Cardiomyopathy**

Twenty-six patients were studied (Table 1). The murmur intensity increased markedly (by 3 of 6 grades) in seven, moderately (by 2 of 6 grades) in eight, and mildly (1 of 6 grades) in three patients with CSR. The increased murmur intensity and the appearance of the typical obstructive contour in the brachial artery pressure tracing with CSP are illustrated in Figures 1 and 2. The murmur did not change in six and decreased in two. In general, the change in murmur intensity to CSP tended to parallel the response in murmur that was observed when the patient abruptly stood up after squatting and during the Valsalva maneuver (Table 2).

Heart rate and blood pressure decreased with CSP in the 18 patients in whom the murmur increased in intensity, in the two patients in whom it decreased, and in two patients in whom it did not change. They did not change in four patients without change in murmur intensity. The murmur was loud (3/6 or 4/6) under control conditions in three of the six patients in whom its intensity did not change and was soft (1/6) in the other three.

Indirect carotid and brachial arterial pressure tracings revealed either the appearance or accentuation of the typical contour of HOCM; i.e., midsystolic trough and late systolic bulge, in all patients in whom the murmur increased in intensity (Fig 2).

Technically adequate M-mode tracings of the mitral valve and left ventricular end-diastolic dimensions were also obtained during CSP in nine patients. In all

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**Figure 1.** Effect of carotid sinus pressure on the murmur of hypertrophic obstructive cardiomyopathy in the standing position. Carotid sinus pressure was applied after the third beat, resulting in immediate slowing and marked increase in murmur intensity. Although the sinus rate returned to control after five beats, the murmur remained very loud, with some variation, for 13 beats. Blood pressure, recorded between beats 6 and 12 of the strip, dropped to 80/60 mm Hg from control value of 120/70 mm Hg. Recording speed, 25 mm/sec.

**Figure 2.** Simultaneous ECG, phonocardiogram, and indirect brachial artery pulse tracing in another patient with documented hypertrophic obstructive cardiomyopathy. With the first beat during carotid sinus pressure-induced bradycardia, the murmur increases in intensity, especially in midsystole, while the brachial artery contour, normal before carotid sinus pressure, appears distinctly obstructive. CSP, carotid sinus pressure; BA, brachial artery pulse tracing.
nine patients, the mitral valve leaflet(s) moved more prominently into the left ventricular outflow tract and/or stayed in that position for a longer period during CSP, indicating an increase in obstruction index (Fig 3). The slope of early mitral valve movement toward the septum was also noted to increase in four patients during carotid sinus pressure, indicating that the leaflets were drawn more rapidly into the outflow tract during the maneuver, presumably because of increased flow velocity (Fig 3). Left ventricular end-diastolic dimension remained unchanged during CSP-induced bradycardia, suggesting that the left ventricular volume did not increase despite the longer pause.

Three patients underwent catheterization. Figure 4 illustrates two representative examples of the events that accompanied CSP during catheterization of the patient shown in Figure 1. In the first two beats recorded in strip A (before CSP), peak systolic pressure was virtually equal in the left ventricle and the femoral artery. With CSP and sinus slowing, left ventricular systolic pressure increased from 114 to 130 mm Hg, while systolic arterial pressure fell from 114 to 92 mm Hg. Systolic left ventricular pressure decreased thereafter to levels even lower than the control values (104 mm Hg), while systolic arterial pressure remained low, with a gradual increase to pre-CSP levels. The peak pressure gradient was 38 mm Hg with the first beat of CSP and gradually decreased with the subsequent beats. Diastolic arterial pressure decreased from 64 to 56 mm Hg immediately with sinus slowing (third beat) and then to 48 mm Hg (fourth beat), but the slope of the diastolic pressure of the 1st beat during CSP was similar to that of the beats prior to CSP; this suggests that the decrease in diastolic pressure was related to the longer diastolic time, and not to excessive vasodilation.

In strip B, a peak pressure gradient of 40 and 60 mm Hg appeared with the second and third beats following CSP, with a gradual decline in subsequent beats. Again, diastolic pressure decreased from 60 mm Hg to 52 mm Hg (fourth beat) and then to 40 mm Hg (fifth beat). In both strips a lower pulse pressure, a deep systolic trough, and a late systolic bulge, all typical of HOCM, appeared in the previously normal arterial pressure tracing, paralleling the appearance of

Table 1—Clinical Characteristics of 26 Patients with Hypertrophic Obstructive Cardiomyopathy (HOCM) and 12 Patients with Hypertrophic Nonobstructive Cardiomyopathy (HNOCM)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>HOCM</th>
<th>HNOCM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr</td>
<td>56±14</td>
<td>62±10</td>
</tr>
<tr>
<td>Men</td>
<td>15</td>
<td>5</td>
</tr>
<tr>
<td>Women</td>
<td>11</td>
<td>7</td>
</tr>
<tr>
<td>NYHA Class 1-2</td>
<td>22</td>
<td>12</td>
</tr>
<tr>
<td>3-4</td>
<td>4</td>
<td>0</td>
</tr>
</tbody>
</table>

Table 2—Response of the Systolic Murmur in 26 Patients with Hypertrophic Obstructive Cardiomyopathy to Carotid Sinus Pressure (CSP) While Standing and to Prompt Standing After Squatting

<table>
<thead>
<tr>
<th>Response to CSP</th>
<th>Increased</th>
<th>Decreased</th>
<th>No change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Response to Prompt Standing After Squatting</td>
<td>16</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Increased</td>
<td>16</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Decreased</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>No change</td>
<td>1</td>
<td>0</td>
<td>4</td>
</tr>
</tbody>
</table>

Figure 3. Simultaneous ECG, brachial artery pulse tracing, and M-mode echocardiogram of the mitral valve in the patient with hypertrophic obstructive cardiomyopathy of Figure 2. With carotid sinus pressure, mitral valve leaflets move more prominently into left ventricular outflow tract and stay completely apposed to the septum for a longer time (arrows). Slope of mitral valve movement toward septum is steeper during carotid sinus pressure, indicating that leaflets are drawn more rapidly into the outflow during the maneuver. Brachial pulse contour also becomes typical of obstruction during complete mitral leaflet-septal apposition in the last beat. CSP, carotid sinus pressure; MV, mitral valve; SEP, septum.
a pressure gradient.

The pressure gradient consistently increased from 100 mm Hg at rest to 160 mm Hg during CSP in the second patient, and from 10 to 50 to 75 mm Hg in the third. The increase in gradient was due to both a decrease in aortic pressure and an increase in ventricular pressure.

Hypertrophic Nonobstructive Cardiomyopathy

Twelve patients with a systolic murmur were studied (Table 1). In 11 patients the murmur remained unchanged. In one patient the murmur increased from 1/6 to 2/6 in intensity. Systolic anterior movement of the mitral valve was not observed at rest or with CSP. The carotid impulse had the typical bifid configuration of HOCM after amyl nitrite administration, but this patient was classified as nonobstructive because of the absence of other findings. On Doppler echocardiography, the gradient increased modestly from 10 to 16 mm Hg with CSP.

Valvular Aortic Stenosis

Thirty-two patients with valvular aortic stenosis were examined. Murmur intensity was unchanged with CSP in 24 patients, although a minimum drop of 20 mm Hg was achieved in their systolic blood pressure and decreased in eight patients. CSP was applied in the supine position during cardiac catheterization to five of the patients. Both left ventricular and aortic pressures decreased, and there was a slight increase in the transvalvular gradient, the maximal change being 10 mm Hg. Left ventricular end-diastolic pressure increased in one and was unchanged in four.

Mitral Insufficiency

The murmur of mitral insufficiency was unchanged in 17 of 23 patients with rheumatic valvular disease or papillary muscle insufficiency and decreased in six. The late systolic murmur of the mitral valve prolapse syndrome decreased in two of eight patients and remained unchanged in six.

Miscellaneous Conditions

The systolic murmur was either unchanged or decreased in 20 patients with prosthetic aortic valves, in one patient with discrete subaortic stenosis and in nine patients with anemia or arteriovenous dialysis shunts.

Analysis

The sensitivity was 69.2 percent when calculated for the 26 patients. If computation is limited to only those 21 patients in whom CSP successfully decreased heart rate and blood pressure, sensitivity is actually higher (85.7 percent). Specificity and positive predictive accuracy were 99 percent and 94.7 percent, respectively.
DISCUSSION

The Murmur of HOCM

This study indicates that the murmur increases in intensity in approximately 85 percent of patients with HOCM in whom CSP slows the heart rate. In contrast, this response in murmur intensity was found in only one of 104 patients with murmurs of different origins. Catheterization data, indirect arterial pressure tracings, and echocardiographic studies indicate that increased left ventricular outflow tract obstruction also accompanies successful CSP.

The presence and nature of the obstruction and the origin of the murmur in HOCM have been the subject of active investigation since the early 1960s, and disagreement persists with respect to the importance of the pressure gradient demonstrated in this disease. It is now generally accepted that the murmur of HOCM originates in the outflow tract, with or without an actually measurable pressure gradient, with an additional component often being due to mitral regurgitation. Recent Doppler studies have confirmed the presence of turbulence in the outflow tract, with less severe or absent turbulence in the left atrium. Angiographic-hemodynamic, Doppler flow, and echocardiographic studies have also proved beyond doubt that obstruction to outflow indeed exists in HOCM. The findings of this study—namely, that increased murmur intensity with CSP-induced bradycardia is associated with clear evidence of increased outflow tract obstruction—agree with and lend additional support to the view that the obstructive component is a major clinical feature in this disease.

Mechanisms of Intensification of the Murmur

An increase in murmur intensity during bradycardia appears at first thought to be paradoxical: the longer diastole would somehow be expected to result in increased left ventricular volume and, therefore, in decreased obstruction at the outflow tract. The current study indicates that this interpretation is too simplistic, and raises serious doubt about the capability of the hypertrophied ventricle of HOCM to accept more blood. We postulate that CSP increases obstruction at the outflow tract and, therefore, murmur intensity by one or by a combination of the following mechanisms: (a) decreased aortic pressure and impedance during the longer diastole; (b) increased force of myocardial contraction associated with the slower heart rate; and (c) increased systolic anterior movement of the mitral valve, provoked by a and/or b and responsible for further obstruction.

Decreased Aortic Impedance

Wigle et al postulated over 20 years ago that the orifice size of the left ventricular outflow tract in HOCM is governed by wall tension (that tends to close the outflow tract) and “distending pressure” (that tends to keep it open) in addition to ventricular volume changes. Any increase in wall tension (ie, from increased contractility) or decrease in distending pressure (ie, from decreased aortic pressure) would bring about a rapid decrease of the orifice size of the outflow tract.

This concept is relevant to the effect of CSP. The very first effect seen with CSP in the three patients who were catheterized was a reduction in end-diastolic aortic pressure just before the beat associated with increased pressure gradient (Fig 4). This decreased aortic pressure, which results from the continuing run-off of blood away from the aorta to the peripheral circulation, represents a critical decrease in the distending pressure at the left ventricular outflow tract, poised at a delicate equilibrium between opposing wall tension and distending pressure: as the aortic valve opens and ejection begins, the musculature of the outflow tract contracts more rapidly and more completely.

Increased Force of Contraction Associated with Slowing of Heart Rate

A second independent mechanism for increased obstruction may be the increased myocardial contraction velocity and force associated with slowing of heart rate. This increased force of contraction would bring about closer apposition of the outflow tract musculature during the first few beats after abrupt slowing of the heart rate. Some authors still maintain that true obstruction does not exist in hypertrophic cardiomyopathy, and the increased murmur intensity with CSP would then have to be explained on the basis of increased flow velocity and turbulence through the outflow tract in the early part of systole. However, the increase in murmur intensity in our patients was characteristically maximal in the middle part of ejection, after the early peak of the carotid upstroke and simultaneous with the midsystolic trough, and not in the first part of ejection. This finding indicates that the increase in murmur intensity is due to more marked obstruction during CSP. This interpretation is further strengthened by the appearance of the typical obstructive pattern in the arterial pulse, both at catheterization (Fig 4) and on indirect arterial pressure tracings (Fig 2).

Increased Systolic Anterior Movement of the Mitral Valve

Carotid sinus pressure resulted in increased extent and/or longer duration of systolic anterior movement of the mitral valve into the left ventricular outflow tract (Fig 3). This indicates increased obstruction during CSP. Indirect evidence of increased flow veloc-
ity in the outflow tract in early systole during CSP is also provided by a comparison of the slopes of systolic anterior mitral valve movement before and during CSP in Figure 3: the slope is distinctly steeper during CSP. This increase in outflow velocity fits well with the present evidence derived from echocardiographic and Doppler studies indicating that obstruction is at least partially due to narrowing of the outflow tract by movement of the mitral valve leaflet(s) into it: the increased early systolic flow velocity during CSP brings about faster and more complete mitral leaflet-septal apposition and more marked obstruction.

The Frank-Starling Phenomenon

A longer cycle during CSP could theoretically allow greater diastolic filling, which would then result in augmentation of contraction force and velocity. Doubt, however, has been expressed about the capability of the hypertrophic, noncompliant ventricle of hypertrophic cardiomyopathy to accommodate a larger volume of blood during a longer diastole, and our own M-mode echocardiographic measurements also suggest that the left ventricular dimensions fail to increase significantly during the longer pause (Fig 3). These observations indicate that the Frank-Starling phenomenon probably did not play an important role in the increased velocity and force of contraction and the augmentation in pressure gradient with CSP, at least in our patients.

Vasodepressor Effect of CSP

The vasodilator effect of CSP theoretically also decreases aortic impedance and increases obstruction. However, this vasodilator response is attributed to indirect withdrawal of peripheral sympathetic tone and, as such, is a delayed phenomenon, usually following the peak of the cardioinhibitory heart rate response. The immediate decrease and stable rate of decline in diastolic blood pressure (Fig 4) indicate that vasodilatation is not instrumental in precipitating the drop of pressure. Once the delayed vasodepressor response to CSP has occurred, however, it may indeed play an important role in maintaining obstruction for several beats even after the negative chronotropic effect of CSP has waned (Fig 4B).

Reduced Murmur Intensity with CSP

As opposed to these enhancing effects on the intensity of the murmur of HOCM, CSP may reduce ventricular contractility to some extent, possibly explaining why the murmur decreased in intensity in two patients with HOCM and in four with valvular aortic stenosis. However, this negative effect of CSP on ventricular contractility, while prominent in the anesthetized animal, is of little consequence in the conscious state. Furthermore, the vagal effect on myocardial contractility is directly related to the preexisting sympathetic tone; the negative inotropic effects of vagal stimulation are certainly least felt at the low sympathetic tone present in the resting state of our patients.

The Clinical Importance of CSP in HOCM

The response of the murmur of HOCM to CSP has not previously been described to our knowledge. The present study suggests that the murmur of HOCM may be unique in its response to CSP: it was the only murmur that increased significantly during this maneuver. The increase in intensity was especially striking when the patients sat or stood, but was also often noticeable in the supine position. The murmur increased somewhat (from 1/6 to 2/6) in one patient classified as nonobstructive who did demonstrate an obstructive element under the influence of the amyl nitrite.

In contrast, the murmur of mitral valve prolapse either remains unchanged or actually decreases in intensity during CSP-induced bradycardia; presumably as diastole becomes prolonged, the left ventricular size increases and mitral valve prolapse and regurgitation decrease.

Maneuvers that are used to influence the murmur of HOCM are not always possible or reliable in the uncooperative or incapacitated patient, and even echocardiography is sometimes technically inadequate. Because of its simplicity, CSP deserves a place as one more diagnostic tool for suspected HOCM. The usual elementary care with the use of CSP in any clinical context is obviously necessary to avoid the rare complications of CSP. We have found that digital pressure on the carotid sinus, without massage, was usually sufficient to induce sinus slowing. The patients whose heart rate did not change with pressure also failed to respond to massage of the carotid sinus.

The relatively low sensitivity (69.2 percent) of the CSP test indicates that it is not possible to rule out HOCM in patients in whom the murmur remains unchanged or decreases. In this respect, it should be emphasized that a positive hemodynamic response to CSP, in the form of decreased heart rate and blood pressure, is a prerequisite for proper evaluation of the response of the murmur. The murmur cannot be expected to change if CSP fails to alter heart rate and blood pressure. The sensitivity of increased murmur intensity in the presence of decreased heart rate and blood pressure is actually higher (18/21 subjects; ie., 85.7 percent). Furthermore, the murmur may not change if obstruction is either maximal or minimal: the human ear may not be able to detect an increase in intensity of a grade 4/6 murmur; alternatively, the increase in obstruction produced by CSP may not substantially increase the turbulence of blood flow in
a nearly maximally or minimally obstructed outflow tract.

We propose that the key element in CSP is the bradycardia it causes. Bradycardia reduces afterload, thus causing a transient increase in velocity and force of ventricular contraction; in addition, sudden bradycardia may independently exert a positive inotropic effect. These lead to increased velocity of blood flow during systole through a narrower outflow tract, more rapid and more complete mitral leaflet-septal apposition, which itself brings about further worsening of obstruction and flow turbulence, and, therefore, an increase in murmur intensity. The high specificity and predictive accuracy of a positive test indicate that a systolic murmur that increases significantly with CSP is likely to represent the murmur of HOCM.

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Murmur of Hypertrophic Obstructive Cardiomyopathy (Klein et al)