How the Left and Right Sides of the Heart, as Well as Pulmonary Venous Drainage, Adapt to an Increasing Degree of Head-Up Tilting in Hypertrophic Cardiomyopathy: Differences from the Normal Heart

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OBJECTIVES
We aimed to assess the differences in the adaptive response of patients with hypertrophic cardiomyopathy (HCM) compared with normal subjects, as well as any association with increased susceptibility to the test.

BACKGROUND
Diastolic function contributes importantly in the adaptation of the normal heart to head-up tilting. This mechanism may be disturbed by an impaired relaxation in HCM.

METHODS
Twenty-one male patients with HCM (46 ± 6 years old) and 22 healthy men (44 ± 8 years) were studied using Doppler echocardiography after 1 and 10 min of head-up tilting at 20°, 40° and 60°.

RESULTS
In control subjects, tilting was associated with 1) a predominance of diastolic pulmonary venous flow and early left ventricular (LV) filling (atrium functioning as an open conduit); 2) right ventricular (RV) shrinkage; and 3) no LV dimensional variations. In patients with HCM, tilting was associated with 1) a prevalence of systolic pulmonary venous flow (atrium functioning as a reservoir in which filling depends on atrial relaxation and compliance) and late diastolic transmitral flow (atrium working as a booster pump); 2) LV shrinkage; and 3) no RV dimension variations. These mechanisms did not prevent stroke volume (SV) from decreasing at 40° and 60° in both groups. Because of a lower increase in heart rate (HR), a reduction in cardiac output (CO) was greater in patients with HCM. The responses were similar after 1 and 10 min of tilting in control subjects, whereas in patients, blood pressure (BP), SV and LV dimension fell more after 10 min.

CONCLUSIONS
Adaptation of the normal heart to tilting is based on a ventricular interaction and LV diastolic properties; HCM relies on left atrial diastolic and systolic functions. An inadequate HR reaction to a fall in BP and SV in HCM (depressed reflexogenic activity) contributes to making CO more vulnerable by greater and more prolonged displacements. (J Am Coll Cardiol 2000;36:185–93) © 2000 by the American College of Cardiology

The hemodynamic basis for syncope or sudden death in hypertrophic cardiomyopathy (HCM) has drawn the attention of many researchers (1–4), and the head-up tilt test is one of the investigative approaches that have been applied (1). A systematic analysis of how patients with HCM adapt to reduced venous return during head-up displacement has never been performed. Nonetheless, there are good reasons for considering it a promising method for expanding our learning of the pathophysiology of HCM, mainly regarding the diastolic function and the reflexogenic autonomic control of the cardiovascular system.

As already emphasized in a previous study performed in normal subjects (5), our understanding of the circulatory adaptation during head-up tilting has been somewhat limited because researchers have generally considered the left ventricle (LV) as synonymous of the whole heart. As a matter of fact, intrinsic to venous return impedance is the concept of involvement of the right side of the heart (6), as well as the pulmonary vascular bed. With this concept in mind, the value of a ventricular interaction (7,8) and pericardial constraint (9,10), of the diastolic properties of the ventricles (5,10,11), can be fully appreciated. Hypertrophic cardiomyopathy is a condition characterized by a predominant alteration in ventricular relaxation and a reduced cardiopulmonary baroreflex sensitivity (12), which would result in adaptation to head-up displacement being basically divergent from normal. This is the background for our interest in a comparative study of patients with HCM versus healthy subjects. The aims were 1) to assess how the pulmonary venous return and left atrial filling patterns in the baseline and subsequent head-up displacement may vary in HCM because of impaired ventricular relaxation; 2) to assess what the difference from the normal heart (11) may be, regarding the mechanism of diastolic ventricular interaction mediated by pericardial constraint; and 3) to assess any association between altered cardiac and reflexogenic
adaptative responses in HCM and an enhanced vulnerability of cardiac output (CO) and blood pressure (BP) by venous return impedance.

**METHODS**

**Patient and control groups and assessment of LV hypertrophy.** We studied 21 men with nonobstructive HCM (mean ±SD age 46 ± 6 years; mean weight 75 ± 9 kg; mean height 171 ± 8 cm). All were suspected of having LV hypertrophy on the basis of a routine electrocardiogram (ECG) or echocardiogram, or both, in the absence of hypertension, valvular disease or any other systemic cause of hypertrophy. Some of the men reported atypical chest pain or mild shortness of breath on exertion. All were newly diagnosed and had never taken cardiovascular medications.

Of the 21 patients, five had an identifiable family history of HCM in a first-degree relative and seven in a second-degree relative. All had regular sinus rhythm and a normal LV ejection fraction at rest (two-dimensional echocardiography according to the Simpson rule). On standard color Doppler velocimetry, no patients had evidence of LV cavity obstruction, five had grade 1 and one had grade 2 mitral regurgitation, as graded subjectively on a scale from 0 (none) to 5 (severe).

End-diastolic LV wall thickness measurements were taken at the onset of the QRS complex, using the leading edge method, and were obtained at separate locations (anterior and posterior septum, anterior lateral and posterior wall) from the parasternal views; the apical views were used to integrate the information obtained in the short-axis images. Measurements from three nonconsecutive beats were averaged, and the maximal ventricular wall thickness from any location was determined. Diagnosis of HCM was considered when maximal LV wall thickness by two-dimensional echocardiography was ≥15 mm (3). Maximal ventricular wall thickness in these patients averaged 17.3 ± 1.2 mm. Coronary angiography was performed in patients with atypical chest pain (n = 9) and ruled out significant epicardial coronary lesions. Patients with apical hypertrophy, as indicated by a spade-shaped ventricular cavity, were not included.

Twenty-two male subjects (control group) were well matched with the patients with HCM in terms of age (44 ± 8 years), weight (76 ± 10 kg) and height (175 ± 6 cm). They had no history of cardiovascular or lung disease, had no diabetes, varicose veins, disturbances of cardiac rhythm or conduction, were nonsmokers, had normal aerobic capacity and could not be considered professional sportsmen. Their physical examination, chest X-ray film, blood chemistry, ECG and echocardiogram were normal; in particular, the presence of cardiac hypertrophy or pericardial effusion could be excluded. Maximal LV wall thickness in this control group averaged 9.1 ± 1.1 mm.

**Head-up tilt test protocol.** Patients and control subjects were subjected to the tilt test between 9:00 AM and 11:00 AM in a quiet, temperature-controlled room (21° to 22°C) after an overnight fast. Heart rate (HR) was monitored continuously, and 15-s ECG recordings (speed 25 mm/s) were obtained at 1-min intervals throughout the study. Blood pressure was determined every minute with the Dinamap system (Critikon, Tampa, Florida), which computes BP of a period of 15 s. For head-up tilting, we used a motorized cantilevered table with foot support; the subjects were not strapped to the table and were instructed to avoid straining their muscles during the tilt.

The following protocol was used: after an initial rest for at least 15 min on the table in the horizontal position, until the heart rate in consecutive minutes varied by no more than 3 beats/min, patients and control subjects were tilted to horizontal angles of 20°, 40° and 60°, for 10 min each with the same ordering. Randomization of the tilt orders in a few patients provided the same results as with tilts ordered from lesser to greater degrees. However, with this method, 60° displacement was less likely associated with muscle strain. Tilting steps were separated by intervals of at least 15 min, during which subjects were returned to a flat position and allowed to reach a steady state before further evaluations were made. Records were taken within the first minute of the initiation of displacement and after 10 min. We did not wish to tilt beyond 60°, because the angle would have required active muscle tension in the subjects.

Among the 25 patients with HCM and the 25 healthy subjects who were originally enrolled in the study, four in the former group and three in the latter group were excluded, because satisfactory pulmonary venous flow velocity throughout the cardiac cycle could not be obtained. Thus, our final groups comprised 21 patients with HCM and 22 control subjects.

**Ultrasound and Doppler recordings.** A phased array echocardiographic Doppler system (Sonos 1500, Hewlett Packard, Palo Alto, California), with a 2.5- or 3.5-MHz transducer for M-mode and two-dimensional echocardiography and a 2.0- or 2.5-MHz transducer for Doppler echocardiography, was used. Two-dimensionally directed M-mode echocardiograms were recorded of the septum and LV posterior wall immediately below the mitral leaflets from a parasternal short-axis window. A two-dimensional apical four-chamber view was also recorded. Combined Doppler ultrasound monitoring was performed by using a
2.5-MHz Doppler imaging transducer. The subjects lay in a very slight left lateral decubitus position (13), and records were made during quiet respiration with paper speed recording velocities of 50 mm/s for flow velocity measurements and 100 mm/s, with simultaneous recording of the ECG and phonocardiogram (with a contact microphone applied to the precordium where the aortic component of the second heart sound was loudest), for isovolumic relaxation time. For ventricular measurements, we used a parasternal long-axis plane, an apical four-chamber plane or a modified position midway between the apex and the parasternal long-axis planes. This last position was mostly used to assess tricuspid valve flow. The sample window was placed just distal to the tips of the open atrioventricular valves, with a minor adjustment made until maximal peak flow velocities were obtained. The velocities of the pulmonary venous flow were examined with the transducer placed at the cardiac apex and were obtained by placing the sample volume 0.5 to 1.0 cm into the upper right pulmonary vein. Care was taken to ensure that the sample volume position remained constant for examination at each HR. Tricuspid inflow was derived from the average of all cycles throughout the respiratory cycle (14). The average of six clear cardiac cycles was taken for pulmonary venous and mitral flow (14) assessment. Left ventricular isovolumic relaxation time was measured from aortic valve closure on the phonocardiogram to the start of the mitral flow.

Echocardiographic and Doppler analysis. With a computer analysis system, the LV posterior and septal endocardial surfaces were digitized at a level immediately below the mitral valve leaflets. The variables obtained included left ventricular end-diastolic dimension (LVEDD) and left ventricular end-systolic dimension (LVESD) and wall thickness. Systolic variables included fiber shortening fraction, calculated as ((LVESD − LVEDD)/LVEDD) × 100; end-systolic wall stress (expressed in dynes/cm²) × 10⁶, calculated as a measure of afterload (15) as end-systolic meridional wall stress = 0.334 × SBP × LVESD/PW(1 + [PW/LVESD]), where SBP is systolic blood pressure and PW is posterior wall thickness; and stroke volume (SV), calculated as the velocity–time integral of the systolic velocity spectrum recorded in the outflow tract of the LV × the subvalvular area of the outflow tract (16). The right ventricular (RV) area at end-diastole was measured from two-dimensional images by using a cine loop display (17).

Off-line quantification of the Doppler recordings was performed with a computer-integrated digitizing pad and specifically designed software to measure time intervals, velocities and velocity integrals. Flow profiles were analyzed by tracing the darkest portion of the spectral printout. For the pulmonary venous flow, we determined peak forward velocities during systole (X) and diastole (Y), Y deceleration time and flow–velocity integrals of systolic and diastolic forward flow waves. The systolic filling fraction of pulmonary venous forward flow was the ratio of the systolic to the sum of the systolic and diastolic velocity integrals. For the atrioventricular valves, peak early inflow velocity (E), peak late atrial velocity (A), the ratio of early to late peak velocity (E/A), early deceleration time and integrated velocities for total E and A filling were measured. The percent total flow–velocity integral contributed by A was also evaluated.

Echocardiographic reproducibility. All measurements were performed in a core laboratory by two senior echocardiographers who read the recordings in blinded manner and without knowledge of the clinical diagnosis. The intraobserver variability (comparing paired readings obtained by the same observer on two separate occasions) and the intraobserver coefficient of variation (comparing results obtained and analyzed by two observers for the same subject) were 7% and 10% for the pulmonary venous flow and 6% and 8% for the transmitial flow, respectively.

Statistical analysis. Data are expressed as the mean value ± SD. Statistical analysis was performed by using two-way repeated measures analysis of variance, Newman-Keuls multiple comparison procedures (post-hoc analysis was not undertaken unless analysis of variance reached statistical significance) and linear regression. Covariate analysis (ANCOVA) was performed for an intergroup comparison of regression lines. A p value <0.05 was considered significant.

RESULTS

None of the patients with HCM or control subjects experienced symptoms or discomfort while supine and during the tilt test. Evaluations were performed after 1 and 10 min of any degree of displacement to assess whether there were any differences between the earlier and later responses. The differences were not significant, with the exception of the 60° displacement in HCM. To simplify the presentation and discussion, reference is made to the results at 10 min.

Baseline data. In the supine position, the patterns of blood flow through the tricuspid valve (Table 1), the mitral valve (Table 2) and the pulmonary veins (Table 3) in patients with HCM were different from those of the control subjects in many respects. In patients, the peak E wave velocity was lower, the peak A wave velocity was higher and the deceleration time was prolonged. These variations were shared by the two sides of the heart. Regarding the pulmonary venous flow, patients showed a greater X/Y ratio, due to a raised X wave velocity and a diminished peak Y wave velocity. The time–velocity integral of the Y wave was also lower and the time–velocity integral and percent total flow–velocity integral of the X wave were greater than normal. Heart rate, BP, SV and CO in the HCM group were similar to those in control group (Table 4). The LVEDD was also similar between the groups, whereas the RV end-diastolic area was smaller in the HCM group.

Tilting data. As compared with supine, tilting produced changes, both in the control subjects and patients with HCM, that involved the RV and LV filling, pulmonary venous flow, HR, BP, SV and CO. Changes occurred with
Table 1. Doppler Echocardiographic Right Ventricular Filling Variables in Control Subjects and Patients With Hypertrophic Cardiomyopathy in the Supine Position and at 10 min of Different Degrees of Head-Up Tilting

<table>
<thead>
<tr>
<th></th>
<th>E Wave</th>
<th></th>
<th>A Wave</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Peak Velocity (m/s)</td>
<td>Deceleration Time (ms)</td>
<td>Time–Velocity Integral (cm)</td>
<td>% Total Velocity Integral</td>
</tr>
<tr>
<td></td>
<td>Control Group</td>
<td>HCM Group</td>
<td>p Value</td>
<td>Control Group</td>
</tr>
<tr>
<td>Supine</td>
<td>0.49±0.10</td>
<td>0.36±0.10</td>
<td>&lt;0.01</td>
<td>200±31</td>
</tr>
<tr>
<td>20° Tilting</td>
<td>0.41±0.09</td>
<td>0.32±0.08</td>
<td>&lt;0.01</td>
<td>210±30</td>
</tr>
<tr>
<td>40° Tilting</td>
<td>0.40±0.09</td>
<td>0.28±0.06†</td>
<td>&lt;0.01</td>
<td>216±40</td>
</tr>
<tr>
<td>60° Tilting</td>
<td>0.38±0.09</td>
<td>0.30±0.07‡</td>
<td>&lt;0.01</td>
<td>230±34</td>
</tr>
</tbody>
</table>

*p < 0.05; †p < 0.01 vs. supine. ‡p < 0.01 vs. immediately lower tilting degree.

A = peak late atrial inflow velocity; E = peak early inflow velocity; E/A ratio = peak early to late inflow velocity; HCM = hypertrophic cardiomyopathy.

an orthostatic stimulus as mild as a 20° displacement and, in several instances, were enhanced by increasing angles of tilting.

RV FILLING (Table 1). In control subjects, head-up displacement, as compared with the flat position, was associated with a reduction of tricuspid E wave peak velocity and time–velocity integral, as well as peak E/A velocity ratio, and with no changes in deceleration time and peak A wave velocity. There was no relation between the magnitude of changes and severity of displacement. In patients with HCM, differences from control subjects while supine persisted at any tilting step and E wave changes with displacement (reduced peak velocity, and time–velocity integral and increased deceleration time) were qualitatively similar to normal, whereas A wave peak velocity was reduced and E/A ratio remained steady. Deceleration time became more prolonged with increasing degrees of head-up displacement.

LV Filling (Table 2). In control subjects, the orthostatic stimulus caused a reduction of mitral E wave peak velocity and time–velocity integral, as well as E/A velocity ratio, and
Table 3. Doppler Echocardiographic Pulmonary Venous Flow Variables in Control Subjects and Patients With Hypertrophic Cardiomyopathy in the Supine Position and at 10 min of Different Degrees of Head-Up Tilting

<table>
<thead>
<tr>
<th></th>
<th>X Wave</th>
<th>Y Wave</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Peak Velocity (m/s)</td>
<td>Deceleration Slope (m²/s)</td>
</tr>
<tr>
<td></td>
<td>Control Group</td>
<td>HCM Group</td>
</tr>
<tr>
<td>Supine</td>
<td>0.49 ± 0.10</td>
<td>0.52 ± 0.09</td>
</tr>
<tr>
<td>20° Tilting</td>
<td>0.37 ± 0.10†</td>
<td>0.49 ± 0.10</td>
</tr>
<tr>
<td>40° Tilting</td>
<td>0.35 ± 0.10†</td>
<td>0.51 ± 0.12</td>
</tr>
<tr>
<td>60° Tilting</td>
<td>0.40 ± 0.10†</td>
<td>0.48 ± 0.10</td>
</tr>
</tbody>
</table>

*p < 0.05; †p < 0.01 vs. supine; ‡p < 0.01 vs. immediately lower tilting degree.

Data are presented as the mean value ± SD.

HCM = hypertrophic cardiomyopathy; X = peak systolic forward flow velocity; Y = peak diastolic forward flow velocity; X/Y ratio = ratio of systolic to diastolic forward velocity.

no changes in deceleration time and peak A wave velocity. In patients with HCM, differences from control subjects while supine persisted at any tilting step; changes in peak E wave velocity with displacement were qualitatively similar to normal, but they were associated with a prolongation in deceleration time and a reduction in the time–velocity integral. Peak A wave velocity was also reduced and the peak E/A ratio remained unchanged. In patients with HCM, changes in deceleration time at 60° were greater than those at less severe displacements.

PULMONARY VENOUS FLOW (TABLE 3). In control subjects, during head-up tilting, as compared with the flat position, the peak velocity and time–velocity integral of the X wave became reduced and those of the Y wave became augmented, resulting in a diminished peak X/Y velocity ratio. In patients with HCM, supine differences from normal persisted at any tilting angle. With the orthostatic stimulus, there was no effect on the X wave peak velocity and time–velocity integral, a reduction of the peak velocity and time–velocity integral of the Y wave and an increase of the X/Y ratio.

Row data traces illustrating the typical pattern of transmural and pulmonary vein flow velocities in the supine position and at 60° tilting for one control subject and one patient with HCM are reported in Figure 1.

VENTRICULAR END-DIASTOLIC DIMENSIONS (FIG. 2). In control subjects, a tilting angle of 20° caused shrinking of the RV diastolic area and no changes in LVEDD. Displacements of 40° and 60° were also ineffective on the left side of the heart, and caused a further reduction of the RV diastolic area. In patients with HCM, however, there were no variations in the RV area at any angle of tilting, an increasing reduction of the LVEDD from 20° to 40° and from 40° to 60° displacement.

SYSTEMIC HEMODYNAMIC DATA (TABLE 4). Both in control subjects and patients with HCM, tilting, as compared with the horizontal position, was associated with increased HR and decreased SV and CO. These variables were similar in the two groups while patients were supine or tilted at a 20° angle. Differences were evident at more severe displacements. In fact, HR and CO at 40° and HR, CO and SV at 60° were significantly lower in patients with HCM than in control subjects. In addition, in the patient group, SV and CO at 1 min of 60° tilting (data not included in Table 4) were similar to those at 10 min of displacement at 40°, but they became significantly lower with prolongation of tilting to 10 min (data included in Table 4). Regarding BP, it is remarkable that a decrease from the supine position of systolic values in HCM was significant at 40° and 60°, and that the diastolic pressure became reduced at 60° instead of rising, as it did in control subjects.

LEFT VENTRICULAR SYSTOLIC PERFORMANCE. When individual values of fiber shortening fraction recorded at baseline and after 1 and 10 min at 20°, 40° and 60° of tilting were plotted against the corresponding LV end-systolic wall stress, the slope of the regression line in HCM was steeper than that in control subjects (p < 0.01, ANCOVA), but figures in either group were distributed along the same regression line. This suggests that changes in posture did not significantly alter the relation between LV afterload and systolic performance, both in normal and hypertrophic hearts. Figure 3 reports the mean values of LV fiber shortening fraction and LV end-systolic wall stress in both groups at the various study steps.
Table 4. Hemodynamic Data in Control Subjects and Patients With Hypertrophic Cardiomyopathy in the Supine Position and at 10 min of Different Degrees of Head-Up Tilting

<table>
<thead>
<tr>
<th>Group</th>
<th>Value</th>
<th>Group</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart Rate</td>
<td>Control</td>
<td>HCM</td>
<td>p</td>
</tr>
<tr>
<td>(beats/min)</td>
<td>65</td>
<td>67</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td></td>
<td>46</td>
<td>48</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Systolic Arterial Pressure (mm Hg)</td>
<td>Control</td>
<td>HCM</td>
<td>p</td>
</tr>
<tr>
<td></td>
<td>120</td>
<td>137</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td></td>
<td>115</td>
<td>128</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Diastolic Arterial Pressure (mm Hg)</td>
<td>Control</td>
<td>HCM</td>
<td>p</td>
</tr>
<tr>
<td></td>
<td>80</td>
<td>81</td>
<td>0.01</td>
</tr>
<tr>
<td></td>
<td>80</td>
<td>81</td>
<td>0.01</td>
</tr>
<tr>
<td>Stroke Volume (ml)</td>
<td>Control</td>
<td>HCM</td>
<td>p</td>
</tr>
<tr>
<td></td>
<td>70</td>
<td>70</td>
<td>0.01</td>
</tr>
<tr>
<td></td>
<td>72</td>
<td>72</td>
<td>0.01</td>
</tr>
<tr>
<td>Cardiac Output (ml/min)</td>
<td>Control</td>
<td>HCM</td>
<td>p</td>
</tr>
<tr>
<td></td>
<td>5,400</td>
<td>5,400</td>
<td>0.01</td>
</tr>
<tr>
<td></td>
<td>5,400</td>
<td>5,400</td>
<td>0.01</td>
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DISCUSSION

The results of this study show, for the first time, to our knowledge, that patients with HCM have a significantly different response to head-up tilting than do subjects with normal hearts.

Horizontal position. In HCM, as compared with normal hearts, the mitral flow velocity curve in the supine position showed a lower E velocity, a higher A velocity and a prolonged deceleration time (10). The contour of the Y wave in both groups was similar to that of the mitral E wave, probably because the diastolic forward flow in the pulmonary vein occurs at a time when the atrium functions more as an open conduit between the pulmonary vein and the LV (18), and the contour of the Y wave depends on the same factors that influence the early mitral flow velocity curve (19). The tricuspid velocity curves in HCM duplicated the alterations of the mitral curves, suggesting that the RV was involved in the same diastolic disturbances as the LV. Cellular disorganization, myocardial scarring and abnormalities of the small intramural coronary arteries constitute a substrate (20,21) for a known diastolic dysfunction in HCM—namely, a decrease in LV compliance and prolonged (or incomplete) LV relaxation (20–23).

Head-up tilting. The importance of the sympathetic nervous reaction as an adaptation to head-up displacement is well established (24,25). However, 20° tilting, although capable of significantly reducing venous return, is not associated with an evident adrenergic reaction (1,5,12), as judged by changes in clinical variables such as HR and BP. Because of this, a 20° degree displacement is a reasonably good means of investigating mechanisms other than the autonomic nervous system, that maintain cardiac filling and output during reduction of preload. At this degree of tilting, control subjects showed a reduction in RV end-diastolic dimension and an increase in Y and a decrease in E wave velocities. A reasonable interpretation of these findings is that the diminished venous return reduced the RV volume and, through the ventricular interaction, moved the pressure–volume relation in the LV from being predominantly mediated through the pericardium (horizontal position) to being mediated by myocardial properties, including, among others, the rate of ventricular relaxation (26,27). This, likely, resulted in a facilitated movement of blood from the atrium to the ventricle; a reduced pressure gradient across the mitral valve (decrease in E wave velocity); and a lowered downstream pressure for pulmonary venous return, which moved mainly to the phase of ventricular diastole (increase in Y wave velocity), during which the atrium functions as an open conduit.

In HCM the RV diastolic area failed to shrink at any degree of head-up displacement. It is hard to discern whether the lack of this mechanism, which is a basic one in normal hearts, was due to the reduced baseline diastolic area, myocardial factors intrinsic to the disease, an insuffi-
cient reduction of impedance to RV ejection or a ventricular interaction mechanism triggered by the LV.

In the presence of impaired diastolic function, which in HCM was definitely unmasked with a reduction in filling pressures (increase in deceleration time in contrast to normal), a joint involvement of the systolic and diastolic properties of the left atrium appears to be essential in assisting the LV to adapt to reduced venous return during head-up displacement. In fact, there was a shift of ventricular filling to the later part of diastole; ventricular inflow became, for the most part, conditioned by the atrial contraction; and forward systolic pulmonary venous flow was dominant. Notably, factors that determine the pulmonary venous forward flow during systole, in addition to RV contraction and descent of the annulus toward the LV apex, include mean left atrial pressure, left atrial compliance and relaxation. Consistent with these interpretations, maintenance of SV in our patients during 20° tilting was associated with no changes in the tricuspid and mitral E/A ratios and with an increase in the X/Y ratio, each of which was reduced by the same tilting degree in healthy subjects.

In normal individuals and patients with HCM, the patterns of ventricular filling and dimensions, as well as of the pulmonary venous flow with 40° and 60° displacement, were qualitatively similar to those already discussed. This suggests that the same cardiac adaptive mechanisms coming into action at lower angles of tilting remain active at more severe changes in posture, even though they are unable, both in healthy subjects and patients with HCM, to fully compensate for more severe reductions of venous return.

A meaningful question is whether there is any difference between these adaptive mechanisms in assisting in ventric-
Obvious limitations include those related to the noninvasive technique for central venous pressure (one cannot be sure that the reduction in central venous pressure by tilting is the same in both groups), detection of the immediate changes that precede achievement of a new steady state, measurement of LV end-diastolic pressure and contractility and Doppler assessment of pulmonary venous flow (14). Invasive measurements were considered to be not justified ethically. Superiority of the transeosophageal approach for records of pulmonary venous flow is well known (29). Measurement at the level of the right superior vein, as generally obtained with the transthoracic method, may not be representative of the left-sided vessels or of vessels draining the lower lobes. To obviate these difficulties as much as possible, we always positioned the transducer and manipulated the ultrasound beam as parallel as possible to the direction of flow. To eliminate peripheral muscle tension, which is a major factor in compensating for changes in posture, we instructed the subjects not to strain their muscles during tilting.

Conclusions. Despite these considerations, it may be reasonably deduced from our results that the heart of patients with HCM adapts to diminished venous return during head-up tilting by a likely reduced baroreflex sensitivity and by cardiac mechanisms (diastolic and systolic function of the left atrium) that are basically different from those of a normal heart (ventricular interaction, diastolic properties of the LV) and probably less effective at more severe and prolonged displacements.

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Figure 3. Left ventricular end-systolic wall stress and fiber fractional shortening in control subjects and patients with HCM. Each symbol represents the mean value in the following conditions: supine (solid square); 20° at 1 min (open diamond); 20° at 10 min (solid diamond); 40° at 1 min (open triangle); 40° at 10 min (solid triangle); 60° at 1 min (open circle); and 60° at 10 min (solid circle). Each bar represents 1 SD.


