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Left Ventricular Systolic Dysfunction During Exercise and Dobutamine Stress in Patients With Hypertrophic Cardiomyopathy

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OBJECTIVES We sought to characterize stress-induced left ventricular systolic dysfunction in patients with hypertrophic cardiomyopathy (HCM).

BACKGROUND Myocardial ischemia and diastolic dysfunction occur in patients with HCM. We hypothesized that, in the setting of transient myocardial ischemia, left ventricular systolic dysfunction occurs during exercise and dobutamine stress.

METHODS We studied 39 patients with HCM but without obstructive symptoms at rest or coronary artery disease. A continuous ventricular function monitor equipped with cadmium telluride detectors (VEST) was used to evaluate left ventricular function during supine bicycle ergometer exercise. Dobutamine stress echocardiography (DSE) was also performed. The left ventricular ejection fraction (LVEF) and regional wall motion were determined from echocardiographic images.

RESULTS Changes in the LVEF correlated between exercise and dobutamine stress ($r = 0.643$, $p < 0.0001$). The LVEF decreased more than 5% at peak exercise in 17 of patients (group II), while the other patients had normal responses (group I). New regional wall motion abnormalities during dobutamine infusion were detected in 18 of 110 (16.4%) segments in group I and 42 of 85 (49.4%) segments in group II. Decreased or unchanged regional wall motion occurred more frequently in hypertrophied segments than in nonhypertrophied segments ($p < 0.0001$). There were significant inverse correlations between the LVEF responses during both stresses and the number of abnormal segments noted during dobutamine stress in all patients (VEST: $p < 0.005$; DSE: $p < 0.0005$). Signs of left ventricular obstruction were observed in 11 of 39 patients during DSE. However, there was no significant correlation between the LVEF response and the dobutamine-induced left ventricular pressure gradient.

CONCLUSIONS Exercise-induced systolic dysfunction occurred in 50% of patients with HCM. In these patients, regional wall motion abnormalities were present in hypertrophied segments. (J Am Coll Cardiol 2000;36:856–63) © 2000 by the American College of Cardiology

Exertional dyspnea and chest pain are common complaints in patients with symptomatic hypertrophic cardiomyopathy (HCM). One cause of these symptoms might be myocardial ischemia, affecting either a portion or all of the left ventricle (LV). Myocardial ischemia without significant coronary artery stenosis in the setting of HCM has been demonstrated by fixed or reversible exercise thallium perfusion defects (1–4), myocardial lactate production during atrial pacing (5) and positron emission tomography (6,7).

If an ischemic process contributes to the clinical manifestations of HCM, LV dysfunction during exercise might provide critical information concerning the pathophysiology of HCM. We have previously demonstrated that the LV ejection fraction (LVEF) decreases during exercise in some patients with nonobstructive HCM using a continuous ventricular function monitor equipped with cadmium telluride detectors (VEST) (8). Although LV functional reserve can be assessed with the VEST, it is difficult to determine whether the abnormal responses occur because of diffuse or focal wall motion abnormalities. However, echocardiographic assessment of the LV may be used to analyze regional wall motion during stress-induced ischemia and has been widely employed for the detection of coronary artery disease (CAD; 9,10). Furthermore, it is possible to measure the intraventricular pressure gradient using Doppler ultrasound (11–13).

In this study we evaluated stress-induced LV dysfunction in patients with HCM. In addition, we compared results obtained by exercise stress and dobutamine stress using VEST and dobutamine stress echocardiography (DSE).

METHODS

Study patients. Forty-five consecutive patients with HCM were considered for entry in the study. The diagnosis of HCM was based on the echocardiographic demonstration of a nondilated, hypertrophied LV in the absence of other cardiac or systemic diseases that could cause LV hypertrophy. Coronary angiography and cardiac catheterization were performed in all of the patients. Six patients were excluded

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Abbreviations and Acronyms

ANOVA = analysis of variance
CAD = coronary artery disease
DSE = dobutamine stress echocardiography
ECG = electrocardiography
EDV = left ventricular end-diastolic volume
ESV = left ventricular end-systolic volume
HCM = hypertrophic cardiomyopathy
LV = left ventricle or ventricular
LVEF = left ventricular ejection fraction
VEST = continuous ventricular function monitor equipped with cadmium telluride detectors

from the study for the following reasons: four patients had entered the dilated phase of HCM, midventricular obstruction at rest was present in one patient, and one patient had undergone pacemaker implantation. The remaining 39 patients (33 men, 6 women; 23 to 74 years of age [mean age: 51 years]) were studied. All patients were in sinus rhythm, had angiographically normal coronary arteries and normal LV systolic function at rest. None of the patients had an LV systolic pressure gradient under basal conditions. Twenty-four patients were in New York Heart Association functional class I, and 15 were in class II. Written informed consent was obtained from all patients. All cardioactive drugs were discontinued at least 24 h before stress testing.

VEST. To evaluate ventricular function during exercise, a continuous radionuclide ventricular function monitor (RRG-607, Aloka, Tokyo, Japan) was used. The VEST system consists of a cadmium telluride detector, preamplifier, portable acquisition unit and battery. The patient's red blood cells were labeled in vivo with 740 to 925 MBq (20 to 25 mCi) of technetium-99m. Electrocardiographic electrodes were positioned to record a standard 12-lead electrocardiography (ECG). With the patient in the supine position; the plastic vestlike garment was placed on the patient's chest, and the VEST detector was positioned over the LV blood pool using gamma camera guideline and locked into the garment. The VEST records sequential 50-ms radionuclide emissions from the LV, and the data are transferred to a laptop personal computer (LT11, NEC, Tokyo, Japan). During data sampling, a beat-to-beat three-point LV smoothed time-activity curve was displayed in real time. A fixed percentage of the background activity (70% of the end-diastolic counts) was used as a baseline. Data were summed at 20-s intervals to calculate the end-diastolic and end-systolic counts. For the calculation of relative LV volume, the resting end-diastolic volume (EDV) in the supine position at the beginning of the study was defined as 100%. All other EDV and all end-systolic volumes (ESV) were calculated relative to the initial EDV.

After a 5-min rest period, patients performed supine bicycle ergometer exercise at an initial workload of 25 W, which was increased by 25-W increments every 2 min. The 12-lead ECG and blood pressure were recorded every min during the test. Criteria for terminating the test included: 1) $\geq$4-mm ST segment depression 80 ms after the J point, 2) severe chest pain or fatigue, or 3) achieving the age-predicted maximal heart rate. All data were recorded within 10 min of the termination of exercise.

Changes in the LVEF during exercise were divided into four types, as described in a previous study (14). In type 1, the LVEF increased by more than 5%, and the increase was maintained during peak exercise. In type 2, the LVEF initially increased by more than 5%, but the increase could not be maintained during peak exercise. In type 3, there was no significant change in LVEF. In type 4 there was a persistent decrease in LVEF >5% until the end of exercise. The 5% cutoff was used because changes in LVEF caused by positioning or other errors was <5% in a previous study (14).

DSE. Routine echocardiographic studies were performed in all patients to identify the regions of LV hypertrophy. Studies were performed using a digital ultrasound system (SSA-380A, Toshiba, Tokyo, Japan) with a 3.7 MHz transducer. After resting images were obtained, dobutamine was administered intravenously at incremental doses of 5, 10, 20 and 30 μg/kg/min at 5-min intervals. Echocardiographic imaging was performed at each dose of dobutamine and recorded on videotape for subsequent analysis. Continuous wave Doppler examination of the LV cavity was performed at each dose from the apical window. The 12-lead ECG and blood pressure were monitored at 1-min intervals. The infusion was terminated after the maximal dose was reached or for one of the following reasons: 1) $\geq$2 mm ST segment depression, 2) development of significant side effects or arrhythmias, 3) achievement of 85% of the age-predicted maximal heart rate, 4) systolic blood pressure >250 mm Hg, or 5) a significant fall in systolic blood pressure (>20 mm Hg) from the baseline.

Echocardiographic analysis. Left ventricular wall thickness at end-diastole was measured by B mode echocardiography. The LV was divided into five segments (anterior wall, septal wall, posterior wall, lateral wall and apical wall; Fig. 1). Hypertrophy was defined as a wall thickness $\geq$15 mm.

Videotaped echocardiographic images were digitized, and a quad screen format (Freeland System; TomTec Imaging System, Boulder, Colorado) was used to compare rest images with stress images in the same imaging planes. Regional wall motion was graded for each segment using the following scale: 0 = dyskinetic, 1 = akinetic, 2 = hypokinetic, 3 = normal and 4 = hyperkinetic. During DSE regional wall motion assessments represent the consensus of two experienced observers who were blinded to the clinical data.

Left ventricular volume was assessed in the same blinded fashion. End-diastolic and end-systolic images from the apical four- and two-chamber views were traced using a Cardio 500 (Kontron, Munich, Germany) image processing computer. The end-diastolic image was defined as the image coinciding with the onset of the QRS complex, and

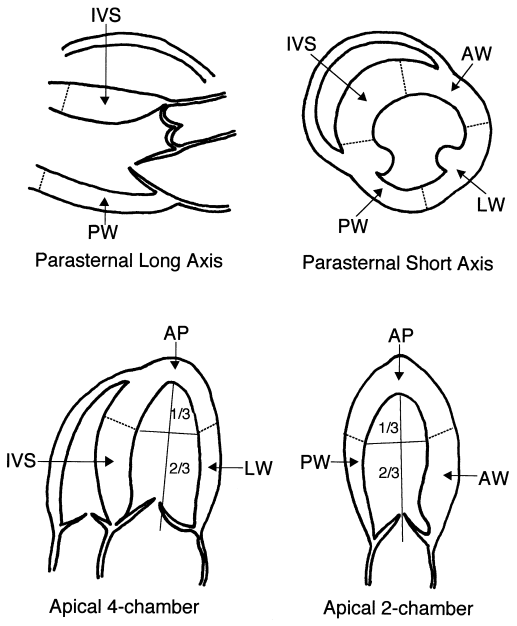

Figure 1. Diagrammatic representation of five-segment regional wall motion analysis in four standard two-dimensional echocardiographic views. AP = apical wall; AW = anterior wall; IVS = interventricular septum; LW = lateral wall; PW = posterior wall.

end-systole was defined as the image with the smallest cavity area. Left ventricular volume and LVEF were calculated from an average of three consecutive cardiac cycles using the biplane Simpson's rule method.

An intraventricular gradient was defined as the development of a late-peaking LV Doppler velocity profile. The pressure gradient was calculated using a modification of the Bernoulli equation: deltaP = $4V^2$, where deltaP is the instantaneous pressure gradient (in mm Hg) and V is the measured maximal flow velocity (in m/s).

Statistical analysis. The results are expressed as the mean ± standard deviation. Differences between groups I and II at baseline were analyzed by Student unpaired *t* test, Fisher exact test and the Mann-Whitney *U* test. Hemodynamic changes during exercise stress and dobutamine stress tests were analyzed using two-way repeated measures analyses of variance (ANOVA). Correlations between different parameters were assessed by linear regression analysis. A p value <0.05 was considered statistically significant. Statistical analyses were performed using the StatView application (version 4.5, Macintosh; Abacus Concepts, Berkeley, California).

RESULTS

Hemodynamic and LV response during exercise. There were significant increases in heart rate, blood pressure and rate-pressure product during exercise. The relative EDV and ESV increased significantly during peak exercise. Therefore, the mean LVEF did not differ significantly between rest (65.8 ± 7.0%) and peak exercise (63.5 ± 12.0%).

However, the individual LVEF responses to exercise were highly variable. Ten patients had the type 1 LVEF response, 14 patients had the type 2 response, 5 patients had the type 3 response, and 10 patients had the type 4 response. Ten patients with the type 4 response and 7 patients with the type 2 response had a decrease in LVEF of more than 5% until they achieved peak exercise. To evaluate stress-induced LV dysfunction in greater detail, patients were divided into two groups. Group I had a normal response, and group II had a decrease in ejection fraction >5%. All patients underwent DSE. Table 1 summarizes the clinical, radionuclide and baseline echocardiographic characteristics of the two groups. There were no significant differences between the groups, except for the proportion of female patients ($p = 0.002$). Chest pain and ischemic ST segment depression during exercise test occurred more frequently in group II (chest pain, $p < 0.05$; ST depression, $p < 0.001$).

Comparison of hemodynamics with exercise and dobutamine stress (Table 2). Although the heart rate, blood pressure, rate-pressure product and LVEF were similar at rest for the two types of stress test, the hemodynamic responses were blunted during DSE compared with VEST. The LV volumes increased during VEST but decreased during DSE ($p < 0.0001$, ANOVA). Although LVEF responses during DSE were smaller than those during VEST, the change in LVEF during DSE significantly correlated with the change during VEST ($r = 0.643$, $p < 0.0001$; Fig. 2).

DSE. The maximum dose of dobutamine (30 μg/kg/min) was infused in 35 patients. Dobutamine infusion was stopped at 20 μg/kg/min because of the development of severe chest pain in two patients, severe palpitations in one patient and hypotension (>40 mm Hg decrease from previous stage) in one patient. In 26 patients (67%), dobutamine administration did not elicit cardiac symptoms. Seven patients (18%) developed angina, and four patients (10%) developed severe palpitations. In two patients, the systolic blood pressure decreased more than 30 mm Hg.

The heart rate, rate-pressure product and EDV indexes during dobutamine stress testing were not different between the two groups (Table 3). The change in LVEF during DSE was significantly different in the two groups ($p < 0.0001$, ANOVA; Table 3, Fig. 3). In group I, the LVEF increased from baseline during low dose (10 μg/kg/min) dobutamine infusion (from 62.1 ± 6.9% to 70.5 ± 8.5%). The increase in LVEF was maintained during the infusion of the maximum dobutamine dose (72.4 ± 10.4%). In group II, the LVEF did not change between baseline and low dose dobutamine infusion (62.5 ± 8.5% and 64.3 ± 8.4%, respectively) but decreased with the maximal dobutamine dose (56.4 ± 9.4%).

New regional wall motion abnormalities developed with dobutamine infusion in both groups (Fig. 4). In group I, the regional wall motion score increased in 78 of the 110 segments analyzed (70.9%) and decreased in 1 of the 110 segments with low dose dobutamine infusion. In group II,

Table 1. Patient Characteristics

	Group I (DeltaEF ≥ −5%)	Group II (DeltaEF < −5%)	p Value
Clinical			
Age (yr)	51.3 ± 12.8	50.2 ± 13.0	0.80
Men/Women	22/0	11/6	0.002
HR at rest (beats/min)	60.8 ± 8.8	61.5 ± 6.2	0.78
SBP at rest (mm Hg)	116.2 ± 16.3	120.7 ± 17.5	0.42
Treatment (n)			0.60
Beta-blockers	2	4	
Calcium channel antagonists	7	5	
Sodium channel antagonists	1	2	
Diuretics	1	0	
No medications	12	8	
Radionuclear			
Exercise duration (s)	503 ± 110	462 ± 132	0.34
HR at peak exercise (beats/min)	128 ± 21	130 ± 23	0.58
SBP at peak exercise (mm Hg)	192 ± 35	178 ± 27	0.18
DeltaLVEF (%)	6.1 ± 7.9	−13.3 ± 7.4	<0.0001
LVEF response pattern (n)			<0.0001
Type 1	10	0	
Type 2	7	7	
Type 3	5	0	
Type 4	0	10	
DeltaST (mm)	−0.5 ± 0.5	−1.4 ± 1.1	<0.001
End point of exercise test (n)			0.077
Chest pain	3	8	0.026
Fatigue	11	6	0.28
Achieved MHR	8	4	0.31
ST depression > 4.0 mm	1	4	0.10
Echocardiographic			
Interventricular septum (mm)	18.5 ± 5.6	18.1 ± 5.4	0.40
Anterior wall (mm)	18.5 ± 4.7	17.3 ± 3.3	0.79
Lateral wall (mm)	14.5 ± 2.4	14.8 ± 3.2	0.29
Posterior wall (mm)	13.9 ± 2.5	13.1 ± 2.4	0.70
Apical wall (mm)	18.3 ± 3.3	16.5 ± 2.1	0.07
LVDd (mm)	44.6 ± 3.8	45.4 ± 5.3	0.61
LVDs (mm)	25.7 ± 3.7	26.0 ± 5.2	0.83
FS	0.43 ± 0.06	0.43 ± 0.07	0.91
LAD (mm)	39.1 ± 5.5	41.4 ± 5.3	0.21
Peak E wave velocity (cm/s)	47.4 ± 12.4	43.1 ± 10.9	0.27
Peak A wave velocity (cm/s)	42.9 ± 10.0	44.2 ± 10.7	0.71
E/A ratio	1.19 ± 0.50	1.04 ± 0.38	0.34
EF (%)	62.1 ± 6.9	62.5 ± 8.5	0.86

Data presented are mean value ± SD or a number of patients.

DeltaLVEF = LVEF at rest to LVEF at peak exercise; DeltaST = ST depression during exercise; EF = ejection fraction; FS = fractional shortening; HR = heart rate; LAD = left atrial dimension; LVDd = left ventricular diastolic dimension; LVDs = left ventricular systolic dimension; LVEF = left ventricular ejection fraction; MHR = maximal heart rate; SBP = systolic blood pressure.

the regional wall motion score increased in 42 of the 85 segments analyzed (49.4%) and decreased in 6 of the 85 segments (7.1%) with low dose dobutamine infusion. These responses were significantly different in the two groups ($p < 0.005$). In group I, the regional wall motion score increased in 1 of 110 segments and decreased in 17 of 110 segments (15.5%) when the dobutamine infusion was increased to the maximum dose. In group II, the regional wall motion score increased in 17 of 85 segments (20.0%) and decreased in 34 of 85 segments (40.0%) when the dobutamine infusion was increased to the maximum dose. These responses were significantly different between the two groups ($p < 0.0001$). The relationship between regional wall motion responses during DSE and ventricular wall hypertrophy are summarized in Table 4. A decrease or no change in regional wall motion score occurred more frequently in hypertrophied segments than in nonhypertrophied segments ($p < 0.0001$). There were significant inverse correlations between the LVEF response during both stresses and the number of dysfunctional segments identified by dobutamine stress (VEST, $p = 0.0016$; DSE, $p = 0.0002$).

Doppler echocardiography during dobutamine stress. During DSE, a late-peaking LV Doppler velocity profile was observed in 11 of 39 patients (28%). In 6 of the 11 patients, systolic anterior motion of the mitral valve occurred during DSE with high peak velocities (>3.0 m/s)

Table 2. Comparison of Hemodynamic Responses Between Exercise and Dobutamine Stress

			p Value (ANOVA)		
	VEST	DSE	Stress Effect	Time Effect	Stress × Time Interaction
HR (beats/min)			0.014	<0.0001	0.0028
Baseline	61.4 ± 5.8	61.1 ± 7.7			
Maximal stress	128.9 ± 21.9	116.1 ± 15.9			
SBP (mm Hg)			<0.0001	<0.0001	<0.0001
Baseline	126.3 ± 19.5	118.2 ± 116.8			
Maximal stress	186.0 ± 32.2	143.6 ± 26.2			
RPP (beats/min·mm Hg·10^3)			<0.0001	<0.0001	<0.0001
Baseline	7.9 ± 1.7	7.3 ± 1.5			
Maximal stress	24.1 ± 6.5	16.7 ± 3.8			
Relative EDV (%)			<0.0001	0.84	<0.0001
Baseline	100	100			
Maximal stress	110.6 ± 6.8	89.4 ± 16.4			
Relative ESV (%)			0.13	0.63	<0.0001
Baseline	34.2 ± 7.2	38.2 ± 8.3			
Maximal stress	40.3 ± 12.4	30.9 ± 13.1			
LVEF (%)			0.83	0.16	0.0008
Baseline	65.8 ± 7.0	62.1 ± 7.6			
Maximal stress	63.5 ± 12.0	67.9 ± 9.0			

Data presented are mean value ± SD.
ANOVA = analysis of variance; EDV = end-diastolic volume; ESV = end-systolic volume; RPP = rate-pressure product. Other abbreviations as in Table 1.

present in the LV outflow tract. In the other five patients, high intracavitary flow velocities developed. There was no significant difference in the pressure gradient determined by the modified Bernoulli equation at the maximum dobutamine dose between the two groups (23.8 ± 14.9 mm Hg for group I vs. 29.1 ± 24.2 mm Hg for group II; p = 0.43). There were no significant correlations between the LVEF response and the pressure gradient (p = 0.18) or the systolic blood pressure response during dobutamine infusion (p = 0.089).

DISCUSSION

Previous studies have demonstrated that a limited exercise capacity is common in patients with HCM and is related to the development of diastolic dysfunction during peak exercise (15–17). However, the LV systolic performance during loading in patients with HCM has not been determined. Furthermore, the use of DSE for the assessment of HCM has only been described in two reports (18,19).

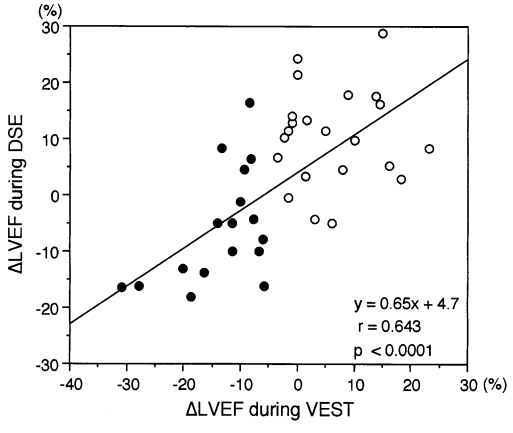

Figure 2. Correlation between the change in ejection fraction during VEST and during DSE. **Open circles** = group I; **closed circles** = group II. DSE = dobutamine stress echocardiography; ΔLVEF = change in left ventricular ejection fraction from baseline to peak stress; VEST = continuous ventricular function monitor.

This study examined LV performance in patients with HCM during exercise or dobutamine stress. The LVEF decreased in about one-half of the patients with HCM during both exercise stress and dobutamine stress testing. In addition, new regional wall motion abnormalities frequently appeared in these patients during DSE.

Global LV systolic function during stress. Manyari et al. (20), using radionuclide angiography, reported that one of five patients with nonobstructive HCM had a decrease in LVEF during peak exercise. Furthermore, three of six patients with latent obstruction and five of seven patients with resting obstruction had a decrease in LVEF during peak exercise. Among our patients, 17 of 39 had a decrease in their LVEF of more than 5%. Although 11 of 39 patients developed latent obstruction during DSE, there was no significant correlation between the LVEF response and the presence of latent signs of obstruction. This discrepancy might be due to differences in patient characteristics, including differences in the severity of the disease.

None of our patients had intracavitary pressure gradients at rest, even with postextrasystolic beats. However, 11 patients developed latent obstruction during high dose dobutamine infusion. The characteristics of obstruction may be different during exercise and during dobutamine stress. In this study, the LV volumes increased during exercise stress but decreased during dobutamine stress. This decrease in LV volume in patients with HCM may have facilitated

Table 3. Hemodynamic Responses During Dobutamine Stress Echocardiography

	Group I (DeltaEF ≥ −5%)	Group II (DeltaEF < −5%)	p Value (ANOVA)		
			Group Effect	Dobutamine Effect	Group × Dobutamine Interaction
HR (beats/min)			0.54	<0.0001	0.87
Baseline	60.8 ± 8.8	61.5 ± 6.2			
Low dose	78.6 ± 13.5	81.2 ± 15.0			
Peak dose	114.8 ± 14.4	117.7 ± 18.0			
SBP (mm Hg)			0.38	<0.0001	0.037
Baseline	116.2 ± 16.3	120.7 ± 17.5			
Low dose	141.0 ± 19.2	132.2 ± 24.0			
Peak dose	148.6 ± 20.5	137.1 ± 31.6			
RPP (beats/min·mm Hg·10^3)			0.71	<0.0001	0.58
Baseline	7.1 ± 1.7	7.4 ± 1.3			
Low dose	11.1 ± 2.8	10.8 ± 3.2			
Peak dose	17.0 ± 2.9	16.3 ± 4.8			
EDVI (ml/m^2)			0.06	<0.0001	0.48
Baseline	42.0 ± 7.8	47.6 ± 13.0			
Low dose	41.4 ± 6.6	46.3 ± 12.7			
Peak dose	36.8 ± 8.9	41.6 ± 10.1			
ESVI (ml/m^2)			0.0044	<0.0001	0.0037
Baseline	16.0 ± 4.2	18.6 ± 8.9			
Low dose	11.7 ± 3.8	16.9 ± 7.7			
Peak dose	10.0 ± 4.4	18.0 ± 7.2			
LVEF (%)			0.0046	0.0002	<0.0001
Baseline	62.1 ± 6.9	62.5 ± 8.5			
Low dose	70.5 ± 8.5	64.3 ± 8.4			
Peak dose	72.4 ± 10.4	56.4 ± 9.4			

Data presented are mean value ± SD.
EDVI = end-diastolic volume index; ESVI = end-systolic volume index; RPP = rate-pressure product. Other abbreviations as in Table 1.

the development of obstruction. Klues et al. (21) demonstrated that LV outflow obstruction in patients with HCM increases after, rather than during, exercise. Furthermore, rapid changes in preload during recovery are most likely responsible for the development of outflow obstruction after exercise. Schwammenthal et al. (22) demonstrated that no significant correlation exists between the resting and exercise pressure gradient in patients with obstructive cardiomyopathy. These reports support the hypothesis that LV obstruction at rest does not always cause the LVEF to decrease with stress.

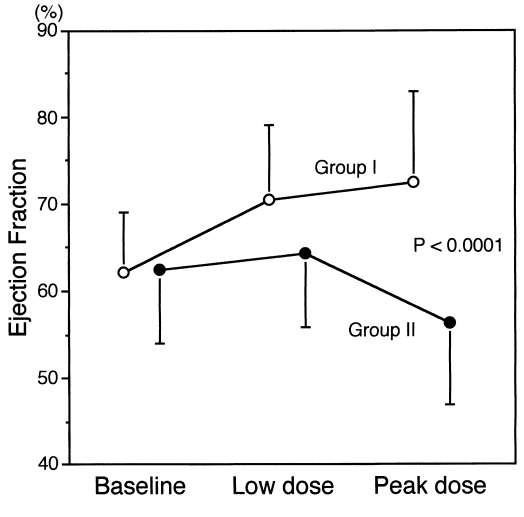

Figure 3. Left ventricular ejection fraction response during dobutamine stress echocardiography in group I **(open circles)** and group II **(closed circles). Circles** and **bars** indicate the mean value ± SD. Data were analyzed by two-way repeated measures analysis of variance (group effect $p = 0.0046$, dobutamine effect $p = 0.0002$, interaction $p < 0.0001$).

There were no significant correlations between the LVEF response and the pressure gradient or the systolic blood pressure response in our patients. These findings suggest that the afterload during stress testing is not always related to the LVEF response in patients with normotensive HCM. However, in this study there were no significant changes in ventricular volumes during dobutamine stress testing in patients in group II with systolic dysfunction although a decrease in the LVEF was observed. The reduced preload reserve in patients with HCM, possibly caused by diastolic dysfunction, may contribute to the decrease in LVEF.

Kawano et al. (23) reported that 4 of 18 patients with nonobstructive HCM had poor ventricular responses (an increase in the fractional shortening ≤7%) during isoproterenol stress echocardiography and that these patients developed systolic dysfunction during isoproterenol infusion. Although they concluded that myocardial ischemia was not the main factor responsible for these findings, we hypothesize that poor LV systolic responses to stress in patients with HCM are due to myocardial ischemia. This is because many of our patients, especially in group II, had exertional angina and ischemic ST segment depression during exercise.

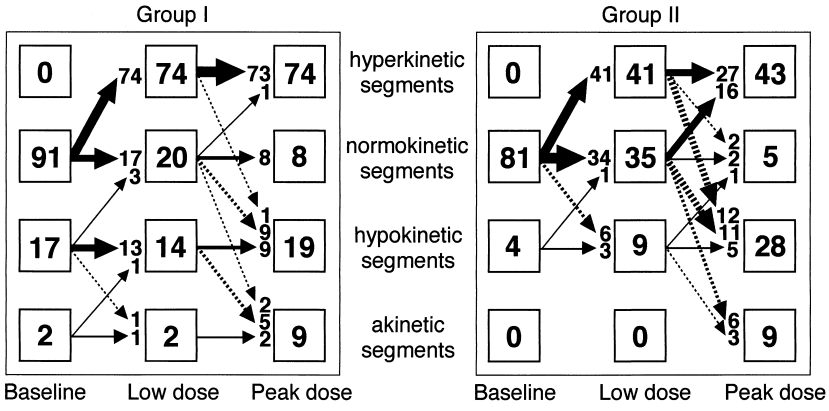

Figure 4. Changes in regional wall motion during dobutamine stress echocardiography. The numbers inside the squares represent the number of myocardial segments. The numbers outside the squares represent the number of segments with changes in regional wall motion from baseline to low dose dobutamine infusion and from low dose to peak dose dobutamine infusion. **Dotted arrows** indicate worsening of wall motion during dobutamine stress echocardiography.

Regional LV systolic function during stress. We hypothesized that the development of myocardial ischemia is the primary reason for the decrease in ejection fraction and the onset of new regional wall motion abnormalities during exercise and dobutamine stress in patients with HCM. Cannon et al. (3) reported that 74% of 30 patients with HCM had reversible thallium defects, and 73% had metabolic evidence of myocardial ischemia during rapid atrial pacing. Furthermore, 19 of these 30 patients developed ischemia during isoproterenol infusion. Previous studies using positron emission tomography have also demonstrated the presence of myocardial ischemia in patients with HCM. Nienaber et al. (7) reported that resting myocardial blood flow is significantly lower in hypertrophied myocardium than it is in nonhypertrophied myocardium and that blood flow and glucose utilization fail to increase during exercise in both hypertrophied and nonhypertrophied segments but become more heterogeneous. Camici et al. (8) reported that dipyridamole-induced coronary vasodilation is impaired in both the hypertrophied and nonhypertrophied myocardium of patients with HCM, especially in patients with a history of chest pain. In contrast, Perrone-Filardi et al. (24) demonstrated that myocardial blood flow is normal in hypertrophied and nonhypertrophied myocardium at rest although the heterogeneity in regional glucose uptake parallels the variability in regional systolic function. These observations are supported by our findings of a decrease in LVEF and the presence of regional wall motion abnormalities during exercise and dobutamine stress in patients with HCM. In our study, the regional wall motion response during DSE was impaired in hypertrophied myocardium, and there was a significant correlation between changes in LVEF and the number of dysfunctional segments. We hypothesize that stress-induced LV systolic dysfunction in patients with HCM is caused by myocardial ischemia occurring predominantly in the hypertrophied myocardium.

Table 4. Association Between Dobutamine Response for Regional Wall Motion and Wall Hypertrophy

	Wall Thickness	
Regional Wall Motion Score	**≥15 mm**	**<15 mm**
Decreased	45	11
Unchanged	16	3
Increased	51	69
		$p < 0.0001$

Study limitations. Dobutamine stress echocardiography has some technical limitations. Specifically, quantitative analysis of regional wall motion was not performed in this study. However, we have previously used digitized images and quad screen format to analyze wall motion in a consistent manner. In this study, DSE produced a lower peak heart rate and systolic blood pressure than exercise stress. These differences suggest a different energy requirement between the two tests, which may affect the cardiac workload in some patients during dobutamine infusion. We did not give atropine during DSE, which has been reported to increase the sensitivity of the test (25). However, there was a close correlation between the two tests with respect to the change in LVEF. Therefore, we believe that LV performance during the two tests was similar.

We did not measure myocardial lactate extraction or coronary blood flow during DSE. New regional wall motion abnormalities that develop during dobutamine stress in patients with CAD reflect myocardial ischemia because dobutamine causes a nonhomogeneous increase in coronary perfusion in patients with CAD (26). However, it is unknown how dobutamine influences coronary circulation in patients with HCM. Lazzeroni et al. (27,28) reported that transient regional dyssynergy dose not occur during high-dose dipyridamole echocardiography in patients with HCM in the absence of CAD. In our patients, regional wall motion abnormalities were commonly observed during DSE. We believe that this difference is mainly due to the fact that dobutamine increases myocardial oxygen consumption more than dipyridamole.

Conclusions. We found that LV systolic dysfunction occurred in 44% of patients with HCM. Furthermore, regional wall motion abnormalities frequently developed during DSE. However, we found no significant correlation between the presence of latent signs of obstruction and stress-induced LV dysfunction. Although the mechanism responsible for these abnormal responses is not clear, we hypothesize that stress-induced ischemia causes transient LV systolic dysfunction.

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