Left Ventricular Functional Reserve in Nonobstructive Hypertrophic Cardiomyopathy: Evaluation by Continuous Left Ventricular Function Monitoring

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The cardiac functional response to exercise in patients with nonobstructive hypertrophic cardiomyopathy (HCM) was evaluated using a continuous ventricular function monitor with a cadmium telluride detector (CdTe-VEST). **Methods:** Supine ergometric exercise was performed under CdTe-VEST monitoring in 41 patients with nonobstructive HCM (34 men and 7 women, age 18–72 yr, mean 51 yr) and 15 patients without cardiac disease (9 men and 6 women, age 36–56 yr, mean 49 yr). **Results:** Although 20 of 41 patients with HCM maintained a LVEF above baseline at peak exercise (Group A), 21 did not show an EF increase at peak exercise (Group B). Exercise duration and work load in Group A were longer and higher, respectively, than in Group B. Resting EF in Group B (72 ± 7.7%) was significantly higher than that in Group A (65 ± 8.2%) and the control group (62 ± 5.9%). The EF increase from baseline to EF overshoot during recovery and the time to EF overshoot were lower and longer, respectively, in Group B than in Group A and the control group. Septal wall thickness and the septum-to-posterior-wall-thickness ratio between Groups A and B were not different. ST-segment depression was observed in all 21 Group B patients and in 8 of the Group A patients. **Conclusion:** In patients with nonobstructive HCM, left ventricular dysfunction during exercise and during recovery was frequently observed but was not related to the degree of septal wall hypertrophy. The CdTe-VEST is a useful means to evaluate left ventricular functional reserve to exercise in patients with HCM.

Key Words: hypertrophic cardiomyopathy; continuous ventricular function monitor; VEST; exercise; left ventricular ejection fraction

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Hypertrophic cardiomyopathy (HCM) is a cardiac disease characterized by increased left ventricular wall thickness and the presence of a nondilated left ventricle without an obvious physiologic explanation (*1*). Abnormal left ventricular function is common, with the diastole especially affected. Although most patients with HCM have normal epicardial coronary arteries, several pieces of evidence suggest that myocardial ischemia may play a central role in the pathophysiology of HCM. For many patients, chest pain is a prominent symptom without significant coronary stenosis. The most convincing evidence for ischemia in HCM is metabolic evidence of anaerobic metabolism during atrial pacing, often in association with findings of inadequate coronary flow reserve (*2–5*). Exercise ^{201}Tl myocardial scintigraphy showed fixed or reversible perfusion defects (*6,7*). Morphologically, fibrous tissue formation in the left ventricular myocardium, ranging from patchy interstitial fibrosis to transmural scars, is found (*8,9*).

If an ischemic process contributes importantly to the clinical manifestations and natural history of HCM, left ventricular functional reserve or dysfunction during exercise might also provide additional critical information about the pathophysiology of HCM. However, few studies about cardiac function during exercise in patients with HCM have been reported (*10,11*). Manyari et al. (*11*) used gated blood pool scintigraphy to evaluate the ejection fraction (EF); however, the interval required for data acquisition is at least 90 to 120 sec. The present study was undertaken to assess precisely the left ventricular functional reserve or dysfunction during exercise using a continuous left ventricular function monitor in patients with nonobstructive HCM, in whom consideration of the effect of systolic pressure gradient on EF during exercise was unnecessary.

MATERIALS AND METHODS

Patient Population

The study group consisted of 41 patients with nonobstructive HCM. There were 34 men and 7 women (age range 18–72 yr, average 51 yr). In each patient, the diagnosis of HCM was based on echocardiographic demonstration of a hypertrophied, nondilated left ventricle in the absence of other cardiac or systemic

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diseases known to cause left ventricular hypertrophy (*1*). A history of chest pain was present in 12 patients.

Coronary arteriographic and cardiac catheterization was performed in 34 of the 41 patients with HCM. Coronary arteriography was normal in each of these 34 patients. There were no findings of a left ventricular systolic pressure gradient under basal conditions, including postextrasystolic beat in any patient. Coronary artery disease was considered unlikely in the remaining 7 patients. Four showed no regional perfusion defect on exercise thallium scintigraphy, and the 3 others had not experienced angina.

A second group, for control purposes, consisted of 15 normal subjects (9 men and 6 women, age range 36–56 yr, average 49 yr). They were patients with atypical chest pain who underwent coronary angiography and treadmill exercise test and were found to have normal coronary anatomy and no ST segment depression during exercise.

Echocardiography

Two-dimensional echocardiographic studies were performed within 1 wk of the radionuclide studies in all patients to identify the distribution of the left ventricular hypertrophy; included were the long-axis, short-axis and apical four-chamber view images. Septal and posterior wall thicknesses were measured in end-diastole using M-mode scans. The presence of left ventricular outflow tract obstruction under basal conditions, including postextrasystolic beat in patients without cardiac catheterization, was estimated from the M-mode echocardiogram based on the magnitude and duration of systolic anterior motion of the mitral valve (*12*). No subject showed outflow tract obstruction.

Continuous Ventricular Function Monitoring During Exercise

To evaluate ventricular function during exercise, the radionuclide continuous ventricular function monitor with cadmium telluride detector (RRG-607, Aloka, Tokyo, Japan) (CdTe-VEST) was used (*13*). Continuous ventricular function monitoring during rest, exercise and recovery was performed by a previously described protocol (*13*). Briefly, after equilibration of 740 to 925 MBq of ^{99m}Tc-labeled red blood cells, 12 electrocardiographic electrodes were attached to the patient's thorax. Then, with the patient in the supine position, the CdTe detector was placed over the left ventricular blood pool under gamma camera control in the left anterior oblique position. After 5 min of rest, supine bicycle ergometer exercise was started of a workload of 25 W and increased by 25 W for every 2 min of stress. Exercise was terminated when either severe chest pain, serious arrhythmia, 0.4 mV or more of ST segment depression 80 msec after the J point and/or fatigue occurred. Systolic and diastolic blood pressures were measured at 1-min intervals during the test. The left ventricular function monitoring was continued for at least 10 min after the termination of exercise. After the completion of the monitoring, the accuracy of the detector positioning was reconfirmed with a 20-sec static image under the gamma camera.

Data Analysis

Prior to data analysis, a trend plot for left ventricular counts over time was displayed to identify significant detector motion, which was represented as a sudden deviation of the plot. After the physical decay-corrected left ventricular time activity curve (50-msec sequential count data) was smoothed by digital filtering, EF was calculated from the stroke counts divided by the background-corrected end-diastolic counts of each beat and averaged every 20 sec. Peak and valley counts of the left ventricular time activity curve were determined as the end-diastolic and end-systolic counts, respectively. Biologic decay correction was not performed because it varied among patients, and the monitoring interval was relatively short (30 min at most). A background correction of 70% of end-diastolic counts was used, based on the authors' previous study, showing an excellent correlation of the left ventricular EF between gamma camera and CdTe-VEST at rest and during exercise (*13*). Relative end-diastolic volume was considered to be 100% at the beginning of the study and, subsequently, was expressed relative to this value. Relative cardiac output was calculated as the relative stroke volume multiplied by heart rate. After the cessation of exercise, EF increased transiently in all patients but two, and peak EF during recovery was defined as EF overshoot (EF-OS). In addition to the EF change from rest to peak exercise, the time period from the cessation of the exercise to EF-OS during recovery and the change of EF from rest to EF-OS were evaluated.

EF response patterns during exercise were divided into four types, as described in the authors' previous study (*13*). In Type 1, EF increased by more than 5% over resting EF until the end of the exercise. In Type 2, EF increased by more than 5% initially but could not be maintained until peak exercise. Type 3 showed no significant EF change (within ± 5% of resting EF). Type 4 revealed a continuous EF decrease of more than 5% until the end of the exercise.

Electrocardiographic abnormalities induced by exercise were considered significant when a further downward displacement of the ST segment of more than 1 mm from baseline occurred (*7*).

Statistical Analysis

Values are expressed as means ± s.d. Comparisons among groups of patients were performed by one-way analysis of variance and the Student's t-test. Differences in proportions were analyzed with the chi-square test. A p value < 0.05 was considered significant.

RESULTS

In the control patients, the resting EF was 62% ± 5.9%. It increased to 75% ± 9.8% at peak exercise and 86% ± 9% at EF-OS during recovery. Fifteen patients showed a Type 1 EF response, and one showed a Type 2 EF response.

Twenty-one of the 41 patients with HCM showed an EF decrease at peak exercise (Group B), and 20 patients demonstrated an EF increase of 0% or more at peak exercise (Group A). No patients had typical anginal chest pain during the exercise. There were no significant differences between the control and Group A patients with respect to any of the hemodynamic and cardiac function parameters at rest or during exercise and recovery. Between the two groups with HCM, heart rate and blood pressure at peak exercise were similar. Resting EF was lower in Group A than in Group B (65% ± 8.2% vs. 72% ± 7.7%, $p < 0.05$), but EF at peak exercise was higher in Group A (74% ± 9.9% vs. 62% ± 10%, $p < 0.001$). Ejection fraction change from rest to peak exercise was higher in Group A than in Group B (8.7% ± 8.9% vs. −10% ± 6.2%, $p < 0.001$). Ejection fraction decreases in all Group B patients were caused by the combination of a mild increase in end-diastolic volume (109% ± 5.7% of baseline value) and a significant increase in end-systolic volume (150% ± 30% of

TABLE 1
Hemodynamic and Cardiac Function Parameters in the Control Group and in Patients with HCM

		Patients with HCM		p Value	
	Control	dEF ≥ 0% (Group A)	dEF < 0% (Group B)	A vs. B	Control vs. B*
Work load (W)	97 ± 25	109 ± 32	89 ± 25	0.05	ns
Exercise period (min)	7.7 ± 1.8	8.7 ± 2.3	7.0 ± 2.0	0.05	ns
Heart rate (bpm)					
At rest	62 ± 12	59 ± 6	61 ± 11	ns	ns
At peak exercise	126 ± 14	121 ± 20	124 ± 19	ns	ns
At EF-OS	94 ± 15	93 ± 17	86 ± 15	ns	ns
BP (mmHg)					
At rest	122 ± 14	123 ± 23	123 ± 16	ns	ns
At peak exercise	182 ± 25	189 ± 35	174 ± 30	ns	ns
At EF-OS	145 ± 19	149 ± 23	143 ± 26	ns	ns
EF (%)					
At rest	62 ± 5.9	65 ± 8.2	72 ± 7.7	0.05	0.001
At peak exercise	75 ± 9.8	74 ± 9.9	62 ± 10	0.001	0.001
At EF-OS	86 ± 9	85 ± 12	83 ± 11	ns	ns
ΔEF (%) from rest					
To peak exercise	13.1 ± 8.0	8.7 ± 8.9	−10 ± 6.2	0.001	0.001
To EF-OS	24.1 ± 7.4	20.2 ± 8.8	11.3 ± 6.4	0.001	0.001
%EDV					
At peak exercise	107 ± 3.8	109 ± 7.1	109 ± 5.7	ns	ns
At EF-OS	102 ± 3.9	104 ± 5.3	105 ± 4.5	ns	ns
%ESV					
At peak exercise	70 ± 21	82 ± 26	150 ± 30	0.001	0.001
At EF-OS	37 ± 22	43 ± 22	54 ± 22	ns	0.05
% Cardiac output					
At peak exercise	263 ± 52	252 ± 49	197 ± 48	0.001	0.001
At EF-OS	216 ± 40	213 ± 42	176 ± 50	0.05	0.05
Time to EF-OS (sec)	76 ± 44	78 ± 50	174 ± 88	0.001	0.001

*There was no significant difference between the control group and Group A.

BP = blood pressure; dEF = EF change from rest to peak exercise; EDV = end-diastolic volume; ESV = end-systolic volume; EF = ejection fraction; EF-OS = ejection fraction overshoot; HCM = hypertrophic cardiomyopathy; ns = not significant.

baseline value). The exercise period was longer in Group A than in Group B (8.7 ± 2.3 vs. 7.0 ± 2.0 min, $p < 0.05$), and maximal work load also was higher in Group A (109 ± 32 vs. 89 ± 25 W, $p < 0.05$). The EF change from rest to EF-OS was higher in Group A (20.2% ± 8.8% vs. 11.3% ± 6.4%, $p < 0.001$) and the time from the end of the exercise to EF-OS was shorter (78 ± 50 vs. 174 ± 88 sec, $p < 0.001$) (Table 1). Ejection fraction values at rest, at peak exercise and at EF-OS during recovery in each patients in Groups A and B are plotted in Figure 1.

All patients had evidence of left-ventricular hypertrophy on resting electrocardiogram. Resting ST-T abnormalities were observed in 13 of 20 Group A patients and 15 of 21 Group B patients (p = not significant). No patients except two (right bundle branch block in one patient each in Groups A and B) had conduction abnormalities at rest and during exercise. ST segment depression developed in all 21 patients with EF decrease at peak exercise and in 8 of 20 patients with EF increase at peak exercise ($p < 0.0001$, Table 2). Septal wall thickness and the septum-to-posterior-wall-thickness ratio in Group A were 17 ± 4.4 mm and 1.43 ± 0.32, respectively. They were similar to those in Group B (19 ± 4.0 mm and 1.64 ± 0.44, Table 3).

Ejection fraction response Types 1, 2, 3 and 4 were demonstrated in 10, 8, 9 and 14 patients, respectively. ST segment depression was noted in only 2 of 10 patients with a Type 1 EF response, in contrast to 6 of 8, 7 of 9 and 14 of 14 patients with Types 2, 3 and 4, respectively ($p < 0.0005$, Table 4). Hemodynamic and cardiac function parameters for each EF response type group are shown in Table 5. Work load, heart rate and blood pressure at peak exercise were similar in the four groups. The exercise period was longer in the patients with Type 1 EF responses than in those with Types 3 and 4, but this difference was not significant (Table 5). Those with Type 1 showed the highest EF increase from rest to peak exercise and to EF-OS, with the shortest time to EF-OS. On the other hand, Type 4 showed the lowest EF increase from rest to peak exercise and to EF-OS with the longest time to EF-OS. Types 2 and 3 demonstrated intermediate values between Types 1 and 4. Septal wall thickness and the septum-to-posterior wall thickness ratio were similar in the four groups (Table 6).

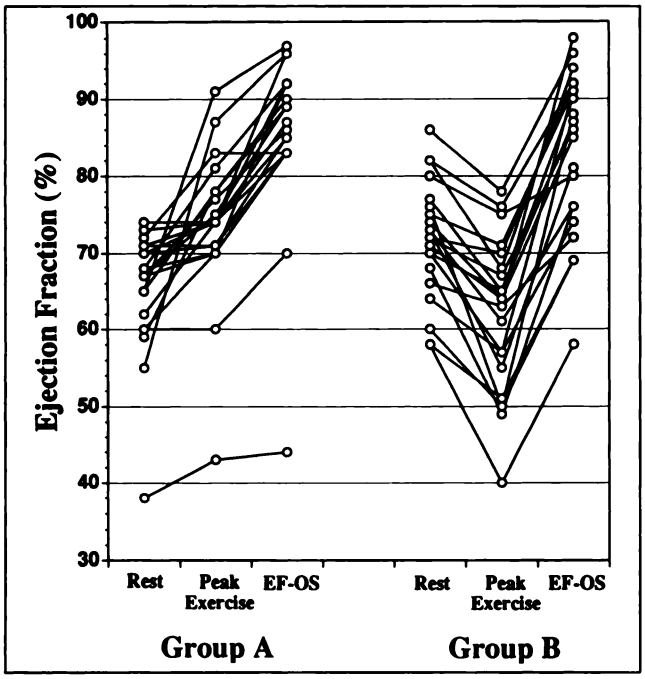

FIGURE 1. Left ventricular EF at rest, at peak exercise and at EF-OS during recovery in patients with EF increase of 0% or more at peak exercise (Group A) and in patients with EF decrease at peak exercise (Group B). Resting EF was lower in Group A than in Group B (65% ± 8.2% versus 72% ± 7.7%, $p < 0.05$), but EF at peak exercise was higher in Group A (74% ± 9.9% versus 62% ± 10%, $p < 0.001$). EF at EF-OS during recovery was similar (Group A = 85% ± 12% versus Group B = 83% ± 11%, p = not significant), however, EF change from rest to EF-OS was higher in Group A (20.2% ± 8.8% versus 11.3% ± 6.4%, $p < 0.001$).

In 29 patients with ST-segment depression, the ST-segment depression started 4.8 ± 2.3 min after the beginning of the exercise. EF at rest, at ST-segment depression and at peak exercise were 70.5% ± 7.3%, 68.7% ± 8.5% and 64.6% ± 10.1%, respectively.

A representative case, a 65-year-old man with HCM, is shown in Figure 2. Ejection fraction started to decrease from the beginning of the exercise because of a slight increase in end-diastolic volume with a significant increase in end-systolic volume. ST-segment depression was observed 3 min after the beginning of the exercise. Ejection fraction increase during recovery (EF-OS) was caused by a rapid decrease in the end-systolic volume with gradual approach of the end-diastolic volume to the baseline value.

TABLE 2
Relationship Between EF Increase from Rest to Peak Exercise and ST-Segment Depression

ST-segment depression	dEF ≥0%	dEF <0%	Total
+	8	21	29
−	12	0	12
Total	20	21	41
		$p < 0.0001$	

dEF = ejection fraction increase from rest to peak exercise.

TABLE 3
Relationship Between EF Increase from Rest to Peak Exercise and Ventricular Wall Thickness

Wall Thickness	dEF ≥0%	dEF <0%	p Value
Septum (mm)	17 ± 4.4	19 ± 4.0	ns
Posterior wall (mm)	12 ± 1.8	12 ± 2.6	ns
Septum/Posterior	1.43 ± 0.32	1.64 ± 0.44	ns

dEF = ejection fraction increase from rest to peak exercise; ns = not significant.

DISCUSSION

The present data revealed that left ventricular dysfunction during exercise is a common phenomenon in patients with nonobstructive HCM. One-half of the patients with nonobstructive HCM demonstrated an EF decrease at peak exercise, and only one fourth of the patients showed an EF increase of more than 5% at the end of the exercise. Exercise radionuclide ventriculography has been used as a sensitive noninvasive test for the diagnosis of coronary artery disease because myocardial function is closely linked to coronary blood flow and dysfunction is an early marker of myocardial ischemia (*14–17*). The cause of left ventricular dysfunction during exercise in patients with HCM may be myocardial ischemia, despite the absence of epicardial coronary artery stenosis. O'Gara et al. (*7*) demonstrated reversible exercise ^{201}Tl perfusion abnormalities in 57% of patients with HCM, which suggests myocardial ischemia induced by exercise. They also showed reversible cavity dilatation on ^{201}Tl study without ventricular volume increase by radionuclide ventriculography in 38% of the patients, which suggests diffuse subendomyocardial ischemia. In addition, Cannon et al. (*5*) revealed that reversible ^{201}Tl perfusion abnormalities during exercise correlated well with metabolic evidence of ischemia during atrial pacing. They further showed that patients with HCM achieved maximum coronary vasodilation and flow at modest increases in heart rate. With continued pacing to a heart rate

TABLE 4
Relationship Between EF Response and ST-Segment Depression

ST-segment depression	EF Response Type 1	2	3	4	Total
+	2	6	7	14	29
−	8	2	2	0	12
Total	10	8	9	14	41
				$p < 0.0005$	

TABLE 5
Hemodynamic and Cardiac Function Parameters in Patients with HCM in Various Types of EF Response to Exercise

	Type of EF response				p	
	1	2	3	4	<0.05	<0.01
Work load (W)	113 ± 21	103 ± 43	92 ± 25	91 ± 27	—	—
Exercise period (min)	9.0 ± 1.7	8.3 ± 2.8	7.0 ± 1.9	7.1 ± 2.3	—	—
Heart rate (/min)						
At rest	58 ± 4	67 ± 14	58 ± 6	59 ± 7	—	—
At peak exercise	119 ± 17	130 ± 25	112 ± 12	128 ± 19	—	—
At EF-OS	93 ± 20	97 ± 18	84 ± 10	85 ± 15	—	—
Blood pressure (mmHg)						
At rest	124 ± 22	124 ± 24	127 ± 22	119 ± 12	—	—
At peak exercise	180 ± 21	193 ± 44	193 ± 36	167 ± 27	—	—
At EF-OS	147 ± 18	155 ± 30	157 ± 26	134 ± 21	—	—
EF (%)						
At rest	64 ± 5.0	68 ± 13	70 ± 5.5	71 ± 8.5	—	—
At peak exercise	79 ± 6.3	67 ± 11	69 ± 5.1	59 ± 10	1 vs. 2	1 vs. 3, 4; 3 vs. 4
At EF-OS	90 ± 5.0	84 ± 17	83 ± 8.0	81 ± 12	—	—
dEF (%)						
From rest to peak exercise	15.4 ± 7.9	−1.1 ± 5.9	−1.1 ± 3.3	−12.4 ± 6.0	—	1 vs. 2, 3, 4; 2, 3 vs. 4
From rest to EF-OS	25.7 ± 8.2	15.4 ± 5.7	12.9 ± 7.2	10.4 ± 5.5	—	1 vs. 2, 3, 4
%EDV						
At peak exercise	109 ± 6.5	111 ± 9.7	110 ± 5.9	108 ± 4.3	—	—
At EF-OS	105 ± 5.3	105 ± 6.2	105 ± 5.2	104 ± 4.1	—	—
%ESV						
At peak exercise	62 ± 21	120 ± 38	113 ± 11	156 ± 29	2 vs. 4	1 vs. 2, 3, 4; 3 vs. 4
At EF-OS	31 ± 16	48 ± 21	54 ± 22	58 ± 23	1 vs. 3	1 vs. 4
% Cardiac output						
At peak exercise	276 ± 49	214 ± 48	210 ± 37	200 ± 54	1 vs. 2	1 vs. 3, 4
At EF-OS	231 ± 41	190 ± 42	180 ± 33	179 ± 57	—	—
Time to EF-OS (sec)	72 ± 48	83 ± 43	125 ± 56	191 ± 100	1 vs. 3	1, 2 vs. 4

dEF = EF change; EDV = end-diastolic volume; ESV = end-systolic volume, EF-OS = ejection fraction overshoot.

of 150 bpm, coronary flow fell with metabolic evidence of ischemia, and elevation of left ventricular filling pressure, probably related to ischemia-induced changes in ventricular compliance, was associated with a decline in coronary flow. Moreover, a paradoxic narrowing of the arteriovenous oxygen difference despite metabolic evidence of ischemia during atrial pacing was found, which suggests a potential mechanism of ischemia in patients with HCM (*4*). Impaired EF response was observed during exercise due to the combination of a slight increase in left ventricular end-diastolic volume and significant increase in end-systolic volume. This volume change during exercise was similar to that found in patients with coronary artery disease in the authors' previous study using CdTe VEST (*13*).

During the early recovery period, a rapid EF increase was observed in all patients but two due to a rapid decrease in end-systolic volume with gradual recovery of end-diastolic volume to the baseline value. This EF-OS was related to the degree of left ventricular dysfunction during exercise; EF-OS was lower and slower in patients with an EF decrease at peak exercise than in patients without EF reduction. This observation was similar to that in the authors' previous study (*13*) in patients with coronary artery disease in whom more severe EF reduction during exercise

TABLE 6
Relationship Between EF Response and Ventricular Wall Thickness

	EF response type				
Wall thickness	1	2	3	4	p
Septum (mm)	17 ± 3.6	15 ± 4.4	19 ± 5.0	19 ± 3.7	ns
Posterior wall (mm)	12 ± 2.1	11 ± 1.2	12 ± 2.4	12 ± 2.7	ns
Septum/posterior	1.41 ± 0.23	1.37 ± 0.41	1.58 ± 0.43	1.70 ± 0.42	ns

ns = not significant.

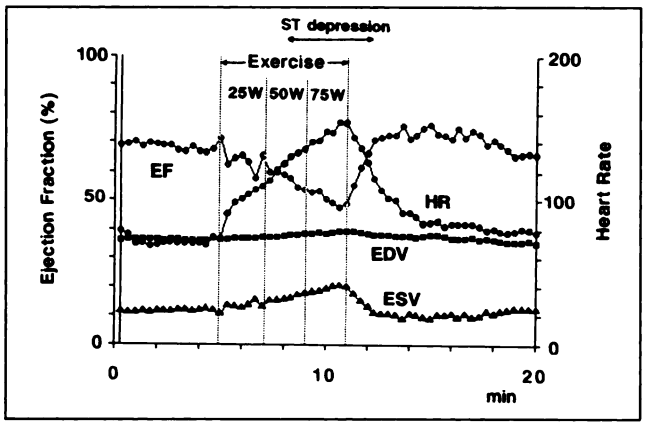

FIGURE 2. Cardiac functional response to exercise in a 65-year-old man with nonobstructive HCM. EF, heart rate (HR), relative end-diastolic volume (EDV) and relative end-systolic volume (ESV) changes were plotted every 20 sec. EF decrease was observed from the beginning of the exercise as a result of a slight increase in EDV and significant increase in ESV. Rapid increase in EF just after the cessation of exercise (EF-OS) was noted.

was accompanied by more delayed and lower EF-OS, which became faster and higher after bypass surgery. This suggested that EF-OS was suppressed by residual ischemia after exercise and may be dependent on the severity of ischemia induced during exercise. In patients with HCM, a similar mechanism could cause delayed and lower EF-OS in patients with EF reduction during exercise, although other factors, such as the changes in preload, afterload and persistent catecholamine-stimulated contractility, might be considered to influence EF overshoot.

In this study, in all 34 patients who underwent cardiac catheterization, no subaortic pressure gradient at rest was present, and it was not provoked in the postextrasystolic beat. In the remaining seven patients who did not undergo cardiac catheterization, no outflow obstruction at basal conditions or in postextrasystolic beat was found. Manyari et al. (*11*) showed that one of five patients with nonobstructive disease had an EF decrease at peak exercise; three of six patients with latent obstruction and five of seven patients with resting obstruction had EF reduction at peak exercise, which suggests different EF responses between patients with and without outflow obstruction. On the other hand, Hanrath et al. (*10*) revealed that two of six patients without outflow obstruction and three of twelve patients with resting or provocative outflow tract obstruction had a stroke volume reduction at maximal exercise. This discrepancy with respect to the cardiac function response to exercise between patients with obstructive and nonobstructive HCM is unclear but might be due to differences in patient characteristics, including different stages in the natural history of the disease. The present study revealed that left ventricular dysfunction during exercise was common in patients with HCM, even in the absence of obstruction. Of 41 patients with nonobstructive HCM, 21 did not show an increase in EF at peak exercise, and 18 patients showed a more than 5% increase in EF during exercise. Only 10 patients maintained EF 5% above baseline until the end of the exercise. The difference in the frequency of functional reserve abnormality in nonobstructive HCM found by Manyari et al. (*11*) and by this study might come from the differences in methods used for analysis and in patient population size and characteristics. Exercise period and work load were significantly shorter and smaller, respectively, in the patients with EF decrease at peak exercise. In the patients with EF decrease at peak exercise, resting EF (72% ± 7.7%) was significantly higher than that of the patients with an EF increase at peak exercise (65% ± 8.2%, $p < 0.05$) and in the control group (62% ± 5.9%, $p < 0.001$). Increased anxiety may have contributed to an EF increase at rest, with a corrective fall in EF to baseline during exercise, but it was unlikely because heart rate and blood pressure at rest were similar among the three groups. Therefore, this finding suggests that the heart with hyperdynamic ventricular function at rest has a decreased functional reserve to exercise. Septal hypertrophy was slightly higher in patients with an EF decrease at peak exercise (septal thickness = 19 ± 4.0 vs. 17 ± 4.4 mm, septum-to-posterior wall thickness ratio = 1.64 ± 0.44 vs. 1.43 ± 0.32), but these differences were not significant. Therefore, the degree of hypertrophy was not considered to be a predictive marker of the ventricular functional reserve to exercise.

Compared with exercise ^{201}Tl myocardial scintigraphy and electrocardial ST-segment depression, Cannon et al. (*5*) reported that 80% of the patients with ST-segment depression showed reversible thallium abnormalities and 70% had metabolic evidence of myocardial ischemia during pacing, whereas 69% of the patients without ST-segment depression had reversible thallium abnormalities and 55% had metabolic evidence of ischemia, which suggests that ST-segment depression is a relatively unreliable marker of myocardial ischemia. In this study, significant ST-segment depression was observed in 29 (71%) of 41 patients. Twenty-one (72%) of 29 patients with ST-segment depression showed EF decrease at peak exercise. All 12 patients without ST-segment depression revealed an EF increase of 0% or more at peak exercise, which suggests the high specificity of the absence of ST-segment depression for apparent left ventricular dysfunction at exercise.

Several pharmacologic interventions for HCM have been evaluated, including calcium antagonists and beta blockers. Verapamil has been shown not only to improve ventricular relaxation and diastolic filling but also to increase exercise tolerance (*10,18,19*). Because the continuous ventricular function monitor can record the continuous changes in left ventricular function during and after exercise, which are difficult to evaluate using conventional gated blood-pool scintigraphy, the continuous ventricular function monitor would be an ideal tool to evaluate more precisely the EF response to exercise and left ventricular functional reserve after pharmacologic treatment. Continuous ventricular function monitoring would be expected to play an important role in elucidating the differences in left

ventricular function during exercise between patients with obstructive and nonobstructive HCM.

The CdTe VEST used in this study has a straight-bore collimator, and so the counts from the left ventricle might be underestimated when the left ventricular volume is large. However, none of the patients in the present study was in the dilated phase of HCM; therefore, no significant underestimation of the count from the left ventricle was considered likely.

In conclusion, one-half of the patients with nonobstructive HCM have an abnormal left ventricular functional reserve or dysfunction during exercise. Although this left ventricular dysfunction was not related to the degree of septal hypertrophy, resting EF was significantly higher in patients with reduced left ventricular functional reserve. The continuous ventricular function monitor can assess dynamic changes in left ventricular function during exercise and recovery and, thus, is useful in predicting reduced left ventricular functional reserve or dysfunction in patients with HCM.

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