

Original article

Exercise Eco-Doppler in Hypertrophic Cardiomyopathy Patients. Determinant Factors of Exercise Intolerance

Gonzalo de la Morena,* Cesar Caro, Daniel Saura, Francisco Marín, Juan R. Gimeno, Josefa González, María José Oliva, Miguel García-Navarro, Angel López-Cuenca, María D. Espinosa, and Mariano Valdés

Servicio de Cardiología, Hospital Universitario Virgen de la Arrixaca, Murcia, Spain

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ABSTRACT

Introduction and objectives: At-rest echocardiography is a poor predictor of exercise capacity in patients with hypertrophic cardiomyopathy. We aimed to test the performance of treadmill exercise Doppler echocardiography in the prediction of functional limitations in these patients.

Methods: Eighty-seven consecutive patients with hypertrophic cardiomyopathy underwent treadmill exercise echocardiography with direct measurement of oxygen consumption. Both at rest and at peak exercise, the mitral inflow, mitral regurgitation, left ventricular outflow tract obstruction and mitral annulus velocities were assessed.

Results: Forty-three patients developed left ventricular outflow tract obstruction during exercise, which significantly decreased oxygen consumption ($21.3 [5.7]$ mL/kg/min vs $24.6 [6.1]$ mL/kg/min; $P=.012$), and had greater left atrial volume ($42.1 [14.5]$ mL/m² vs $31.1 [11.6]$ mL/m²; $P<.001$) and a higher degree of mitral regurgitation and E/E' ratio during exercise. Exercise variables improved the predictive value of functional capacity (adjusted R² rose from 0.38 to 0.49). Independent predictors of oxygen consumption were age, left atrial volume, E/E' ratio and the presence of left ventricular outflow tract obstruction. In a subset of patients without left ventricular outflow obstruction, only left ventricular and atrial volume indexes were independent predictors of exercise capacity.

Conclusions: In patients with hypertrophic cardiomyopathy, left ventricular outflow tract obstruction and left atrial volume are the main predictors of exercise capacity. Exercise echocardiography is a better predictor of functional performance than at-rest echocardiography, although its predictive power is under 50%. In nonobstructed patients, left atrial and ventricular volumes were the independent factors.

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Eco-Doppler de ejercicio en pacientes con miocardiopatía hipertrófica. Factores determinantes de la limitación funcional

RESUMEN

Introducción y objetivos: En pacientes con miocardiopatía hipertrófica, los datos ecocardiográficos en reposo han mostrado una pobre correlación con la capacidad de ejercicio. Investigamos si la ecografía Doppler de esfuerzo podría explicar mejor la limitación funcional.

Métodos: Estudiamos a 87 pacientes consecutivos, remitidos para test cardiopulmonar y ecografía de esfuerzo. Se realizó estudio basal y en el pico de ejercicio para evaluar el gradiente máximo, la regurgitación mitral y las velocidades diastólicas mitral y del Doppler tisular del anillo.

Resultados: Desarrollaron obstrucción con el ejercicio 43 pacientes. Estos alcanzaron un menor consumo de oxígeno ($21,3 \pm 5,7$ frente a $24,6 \pm 6,1$ ml/kg/min; $p = 0,012$), presentaban mayor volumen auricular izquierdo ($42,1 \pm 14,5$ frente a $31,1 \pm 11,6$ ml/m²; $p < 0,001$) y desarrollaron más regurgitación mitral y mayor relación E/E' con el ejercicio. Los datos de ejercicio mejoraron el poder predictivo de la capacidad funcional (R² ajustada = 0,49 frente a R² ajustada = 0,38 en reposo). La edad, el volumen auricular izquierdo, la relación E/E' con el ejercicio y la obstrucción fueron los factores independientes asociados con la capacidad funcional. En los pacientes sin obstrucción, los volúmenes de las cavidades izquierdas fueron los factores determinantes.

Conclusiones: En pacientes con miocardiopatía hipertrófica, la obstrucción con el esfuerzo y el volumen auricular izquierdo son los principales determinantes de la limitación funcional. Los parámetros diastólicos de esfuerzo mejoran la predicción de la capacidad funcional, aunque su poder predictivo no supera el 50%. En pacientes sin obstrucción, los volúmenes de las cavidades izquierdas son los factores determinantes.

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* Corresponding author: Diagonal 12, 30110 Churra, Murcia, Spain.

E-mail address: gdlmorena@yahoo.es (G. de la Morena).

Abbreviations

HCM: hypertrophic cardiomyopathy
 LV: left ventricle
 LVOT: left ventricular outflow tract
 VO₂: oxygen consumption
 VO_{2max}: maximum oxygen consumption

INTRODUCTION

Exercise intolerance is the most common symptom in patients with hypertrophic cardiomyopathy (HCM).^{1,2} The majority of patients are incapable of increasing their oxygen consumption (VO₂) during exercise as the result of an inability to increase systolic volume.^{3,4} Left ventricular outflow (LVOT) tract obstruction, mitral regurgitation, prolonged isovolumetric relaxation, and an increased stiffness of the ventricular chamber are the underlying pathophysiologic mechanisms.^{3–6}

Doppler ultrasound evaluation of these patients facilitates an estimation of the gradient in the LVOT, mitral regurgitation, and filling pressures.^{7–11} However, in patients with HCM at-rest Doppler indexes have been shown to be poorly correlated with capacity for exercise and left atrial pressure^{12–15} and, during exercise, the mechanisms involved can be different for each patient. Some patients suffer significant obstruction that is not present at rest or increases with exercise when various levels of mitral regurgitation are present.⁶ On other occasions, diastolic dysfunction is the primary limiting mechanism.⁴

The majority of studies performed until now have attempted to correlate Doppler ultrasound values in at-rest tests with exercise test results. Few studies have compared exercise Doppler ultrasound values with maximum oxygen consumption (VO_{2max}) and none have considered obstruction as an independent qualitative value in the pressure gradient reached during exercise.

Our study combines cardiopulmonary test results with expired gas analysis and Doppler ultrasound during exercise in order to describe exercise-induced changes in Doppler fluctuations and determine which factors are involved in functional limitations experienced by patients with and without LVOT obstruction.

METHODS

Study Population

We examined a consecutive cohort of patients with HCM who were referred to our hospital for Doppler ultrasound during exercise and cardiopulmonary tests. HCM was diagnosed in the presence of nondilated hypertrophic left ventricle (LV) with a maximum thickness of ≤15 mm in index cases or >12 mm in their family members, and with no other possible cause.¹⁶

We performed a complete clinical evaluation of all patients, an at-rest Doppler ultrasound analysis (with tissue Doppler), and a stress test. Two-dimensional and M-mode measurements, as well as the Doppler analysis, were carried out using a Sonos 7500 ultrasound system (Philips Medical Systems; Andover, Massachusetts, United States). Baseline values and those following exercise were taken with the patient in left lateral decubitus, and were stored digitally for review and analysis using the Xcelera system (Philips Medical Systems; Andover, Massachusetts, United States). All measurements were then analyzed by the same individual,

blinded to the stress test results. For each measurement, 3 different cardiac cycles were averaged, in accordance with the American Society of Echocardiography guidelines.¹⁷

All patients gave informed consent to perform the test and the study protocol was approved by our clinical research ethics committee.

At-rest Doppler Ultrasound

LV wall thickness was measured in the short axes of the LV at the mitral valve and papillary muscles in order to obtain maximum wall thickness. The LV ejection fraction was calculated using the Simpson method. Mitral Doppler readings were obtained from the apical 4-chamber view, placing the volume sample at the edge of the mitral leaflets. Peak E-wave and A-wave velocities were averaged in 3 consecutive cycles. Mitral ring velocities were obtained using tissue Doppler placing the volume sample in the lateral/septal ring. We obtained 3 to 5 cycles and averaged 3 for the early (E') and late (A') diastolic waves, as well as for an evaluation of diastolic intervals. In accordance with the classification system by Garcia et al.,¹⁸ we established 4 different filling patterns in mitral flow: normal, prolonged isovolumetric relaxation, pseudonormal, and restrictive. The LVOT was measured using color-guided continuous wave Doppler. We considered obstructive entities those that reached a gradient >30 mmHg in the stress test. The classification of mitral regurgitation was based on the planar analysis of the regurgitating surface: mild (1–4 cm²), moderate (4–8 cm²), and severe (>8 cm²). Left atrial volume indexed for body surface area was obtained using the 2-plane Simpson method (mL/m²).¹⁹

Cardiopulmonary Test

Following the baseline Doppler ultrasound examination, we administered a stress test limited to the symptoms present, using a treadmill following the Bruce protocol. Patients were urged to exercise until exhaustion. Heart rate, blood pressure, and a 12-lead electrocardiogram were monitored and registered at rest, every 2 min during exercise, and 5 min after exercise. Gas exchange values and ventilation parameters were obtained using a pneumotachograph and CPX System analyzer (Medical Graphics Corp.; St. Paul, Minnesota, United States), calibrated as necessary before each test. The VO₂, VCO₂, and other ventilatory parameters and calculations were determined during each respiration and averaged every 10 s. Before starting the test, the respiratory exchange rate had to be ≤0.85. VO_{2max} was established as the highest value of the 10-s averages during the last minute of exercise (in mL/kg/min). Functional capacity was determined as the percentage of the observed maximum VO_{2max} as compared to the theoretical maximum value based on age, sex, and body surface area.²⁰ The criteria for interrupting the test were exhaustion, severe arrhythmia, severe hypertension (systolic >240 mmHg or diastolic >110 mmHg), hypotensive response (>20 mmHg), or limiting symptoms. We defined an abnormal pressure response as an increase <25 mmHg or a drop >10 mmHg during exercise.²¹

Stress Echocardiogram

When any of the interruption criteria for the test was reached, the patient was rapidly placed on a gurney, in the same left lateral decubitus position as before. We then recorded 2 cycles of the apical 4-chamber view, 2-dimensional color images, 5 continuous Doppler LVOT cycles, pulsed mitral Doppler, and tissue Doppler of the lateral/septal ring. All images were taken 1 min after peak

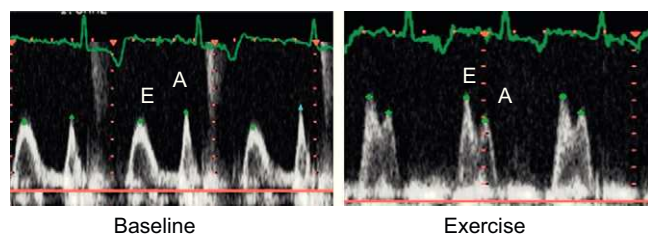


Figure 1. Mitral flow at rest (A) and after exercise (B) in patients with a prolonged isovolumetric relaxation pattern at rest, which becomes pseudonormal during exercise, either an inverted E/A ratio.

exercise. We considered pseudonormalization of diastolic flow induced by exercise as the change from a prolonged at-rest relaxation pattern to a pseudonormal or restrictive pattern with exercise (Fig. 1).

Statistical Analysis

We used the Kolmogorov-Smirnov test to determine whether each variable exhibited a normal distribution. Variables with a normal distribution were expressed as mean (standard deviation), and those without a normal distribution were expressed as a median [interquartile range]. Qualitative variables were expressed as percentages. The differences between groups were compared using chi-square, Mann-Whitney U, Student *t* tests or analyses of variance, as appropriate. To evaluate the relationship between variables and VO_2 we used Pearson's and Spearman's correlation coefficients. We used a backwards multiple regression analysis to determine which independent factors were associated with functional capacity, expressed as percentage of VO_{2max} . We introduced variables with a significant association resulting from the simple analysis ($P < .05$) into the model. We used two different models: one with echocardiographic and at-rest Doppler values and another including all variables for both at-rest and exercise tests. In addition to analyzing the overall patient group, we assessed patients with and without obstruction separately to determine the independent predictors for one presentation of the disease or another. We considered a P -value $< .05$ as statistically significant. For the statistical analysis, we used SPSS statistical software, version 13 (SPSS, Inc.).

RESULTS

Baseline Characteristics and Stress Test

In total, we registered 103 patients referred to our department for stress tests including VO_2 and Doppler ultrasound during exercise; 16 were excluded due to persistent atrial fibrillation. Therefore, the study included 87 patients (29 female; mean age 51.1 [16.4] years) (Table 1). The majority of patients (43.9%) had functional class II according to the New York Heart Association scale; no patients had undergone operations or alcohol septal ablation previously, and 9 patients carried pacemakers.

Patients walked for a mean 7.15 (2.4) min, the maximum heart rate was 130.1 (25.8) bpm, and the respiratory exchange rate reached 1.01 (0.08). There were no observable complications. One patient suffered a paroxysmal atrial fibrillation at peak exercise, with spontaneous reversion during the first minute of recovery. An abnormal pressure response was observed in 23 patients, although only one of them was hypotensive. Ten of these patients were under treatment (7 with beta blockers and 3 with calcium antagonists).

Table 1

Clinical and Echocardiographic Characteristics of the Study Population (n=87)

Age, years	54.3±13.1
Male	58 (66.7)
NYHA functional class	
I	22 (25.2)
II	39 (44.8)
III	26 (29.9)
MWT, mm	20.5±5.4
LVD, mm	43.2±7.3
LAVI, mL/m ²	36.9±14.3
At-rest gradient>30 mmHg	23 (26.4)
LVEF, %	65.9±9.1
Pacemaker	9 (10.3)
Defibrillator	7 (8.0)
Medication	
Beta blockers	38 (43.6)
Calcium antagonists	18 (20.6)
Disopyramide	10 (11.5)
Family history of HCM	28 (32.2)
Family history of sudden death	8 (9.9)

LAVI: left atrial volume index; LVD, left ventricular telediastolic diameter; LVEF, left ventricular ejection fraction; HCM, hypertrophic cardiomyopathy; MWT, maximum wall thickness; NYHA, New York Heart Association. Variables expressed as mean±standard deviation or no. (%).

Exercise Ultrasound

The results from the ultrasound stress tests are summarized in Table 2. We did not observe segmental abnormalities in the induced contractility during exercise. The LV ejection fraction increased from 65.9 (9.1)% (range: 53%–85%) to 71.5 (9.1)% (range: 57%–85%) ($P < .001$).

In general, mitral and ring flow velocities increased with exercise (Table 2). There were significant increases in E-wave and A-wave values, but the E/A ratio was constant. We also observed a proportional increase in ring E' wave values with no differences in the E/E' relationship after exercise as compared to baseline values.

Mitral Filling Pattern

In some patients, we observed that exercise deteriorated mitral filling patterns (Table 2). At rest, 14 of the 41 patients with a prolonged isovolumetric relaxation pattern developed a pseudonormal or restrictive pattern with exercise (Fig. 1). This pseudonormalization was associated with a greater left atrial volume indexed for body surface area (47.3 [14.6] mL/m² vs 32.4 [14.5] mL/m²; $P < .05$), worse functional capacity (66.5 [11.4]% vs 81.8 [20.8]%; $P < .05$), higher E/E' ratio following exercise (19.4 [7.9] vs 12.5 [6.4]; $P = .015$) and more frequent mitral regurgitation following exercise (71.4% vs 25.9%; $P < .01$).

Left Ventricular Outflow Tract Obstruction

At rest, 23 patients experienced obstruction (31.5%), and another 20 patients developed gradients >30 mmHg with exercise. These 43 patients compose the group with obstructive patterns. Patients with obstruction had more dilated left atria and a greater wall thickness (Table 3). Patients with obstructive patterns had a higher mitral regurgitation value and E/E' ratio at rest and after exercise. The VO_{2max} (in mL/kg/min or as functional capacity) of patients with obstruction was significantly lower than in nonobstructed cases (Table 3).

Table 2
Echocardiographic Evaluation While at Rest and After Exercise

Variable	Rest	Exercise	P
Gradient >30 mmHg	23 (26.4)	43 (49.4)	<.001
Maximum gradient, mmHg	58.8±23.9	69.8±35.1	<.001
LVEF, %	65.9±8.8	71.2±9.1	<.001
E, cm/s	72.9±22.1	93.7±30.6	<.001
A, cm/s	66.2±21.5	88.1±32.1	<.001
E/A	1.24±0.65	1.24±0.70	.92
QE, ms	457.2±56.8	338.1±96.4	<.001
QE', ms	499.8±118.4	400.0±124.3	<.001
IVRT, ms	116.6±38.4	89.3±34.4	<.001
Septal E', cm/s	5.2±2.2	7.4±3.1	<.001
Lateral E', cm/s*	6.7±2.9	8.9±5.8	<.001
Septal E/E'	15.5±6.1	15.1±7.9	.47
Lateral E/E'	11.5±5.8	9.9±4.7	.03
Filling pattern			<.001
Normal	24	12	
Prolonged isovolumetric relaxation	41	41	
Pseudonormal or restrictive	22	34	
Mitral regurgitation	19 (21.8)	34 (39.1)	<.001
Mild	16	24	
Moderate	3	9	
Severe	0	1	

IVRT, isovolumetric relaxation time; LVEF, left ventricular ejection fraction; QE, time between mitral E-wave and Q-wave; QE', time between septal E'-wave and Q-wave.

Values expressed as mean±standard deviation or no. (%).

* Data available for 36 patients.

Determinant Factors of Functional Capacity

Table 4 shows the correlations between the different variables and VO_{2max} . An obstruction at the peak of exercise >30 mmHg was correlated with VO_2 ($r=-0.384$; $P<.001$). However, we did not observe a significant relationship between VO_2 and maximum gradient at rest or at exercise. Age ($r=-0.28$; $P=.001$), sex ($r=-0.52$; $P<.0001$) and left ventricular and atrial volume were correlated with VO_2 . As regards Doppler parameters, the lateral/septal E/E' ratios and time between mitral E wave and Q-wave (QE interval) were significantly correlated with VO_2 , both at rest and upon exercising (Fig. 2). An increase in the septal ring E' wave ($r=0.396$; $P=.001$) was associated with a higher VO_2 .

In the multiple regression analysis, the model including at-rest variables yielded an adjusted R^2 of 0.379, and the only factors independently associated with functional capacity were sex ($P=.001$) and left atrial volume ($P=.001$). The model that included both at rest and exercise variables showed an adjusted R^2 of 0.49. In this model, the independent factors were age, left atrial volume index, obstruction during exercise, and E/E' and E/A ratios after exercise (Table 4). In obstructive cases, these same variables also were independently associated with functional capacity, with a predictive value >50% (adjusted $R^2=0.53$). In nonobstructed cases, the determining factors for functional capacity were left atrial and ventricular volumes (adjusted $R^2=0.39$).

DISCUSSION

Our study shows that the obstructive forms of HCM cause a greater functional limitation than do nonobstructive forms,

Table 3
Comparison Between Patients With and Without Left Ventricular Outflow Tract Obstruction

Variable	Obstruction (n=43)	No obstruction (n=44)	P
At rest			
Age	49.9±17.3	52.3±15.6	ns
Male	32	26	ns
LVD, mL	82.1±25.8	80.4±26.6	ns
LVEF, %	67.5±8.8	65.1±8.7	<.001
LAVI, mL/m ²	42.1±14.5	31.1±11.6	<.001
MWT, mm	21.8±5.2	18.9±5.2	.012
E, cm/s	80.9±23.4	65.4±17.7	.001
A, cm/s	73.5±22.5	60.6±21.1	.007
E/A	1.20±0.55	1.27±0.73	ns
Septal E', cm/s	4.73±1.84	5.58±2.44	ns
Septal E/E'	18.6±7.3	12.9±4.5	<.001
Exercise			
Exercise, min	7.09±2.4	7.10±2.2	ns
Bruce stage	2.77±0.77	3.09±1.03	ns
VO_{2max} , mL/kg/min	21.3±5.7	24.6±6.1	.012
Percentage VO_2 , %	66.1±14.2	80.4±20.1	<.001
E, cm/s	106.5±29.8	81.4±26.3	<.001
A, cm/s	93.4±32.2	83.1±31.6	ns
E/A	1.28±0.55	1.20±0.80	ns
Septal E', cm/s	7.14±3.2	7.49±2.98	ns
Septal E/E'	13.9±5.8	9.5±5.0	.01
Mitral regurgitation	25 (58.1)	9 (20.4)	<.001
Mild	15	9	
Moderate	9	0	
Severe	1	0	

LAVI, left atrial volume index; LVD, left ventricular telediastolic volume; LVEF, left ventricular ejection fraction; MWT, maximum wall thickness; ns, not significant; VO_2 , oxygen consumption; VO_{2max} , maximum oxygen consumption.

Data are expressed as mean±standard deviation or no. (%).

Table 4
Variables Associated With Maximum Oxygen Consumption. Univariate Analysis

Variable	R	P
Age	-0.276	.001
Female	-0.522	.001
LAVI	-0.312	.004
LVD	0.034	.002
MWT	-0.280	.009
At-rest variables		
Septal E/E'	-0.397	.01
Lateral E/E'	-0.515	.001
QE	-0.329	.004
Exercise variables		
Gradient >30 mmHg	-0.384	<.001
Septal E'	0.401	.001
Lateral E'	0.479	.001
Septal E/E'	-0.515	.001
Lateral E/E'	-0.509	.001
QE	-0.312	.008
Increase in septal E' velocity	0.396	.001

LAVI, left atrial volume index; LVD, left ventricular telediastolic volume; MWT, maximum wall thickness; QE, time between mitral E-wave and Q-wave.

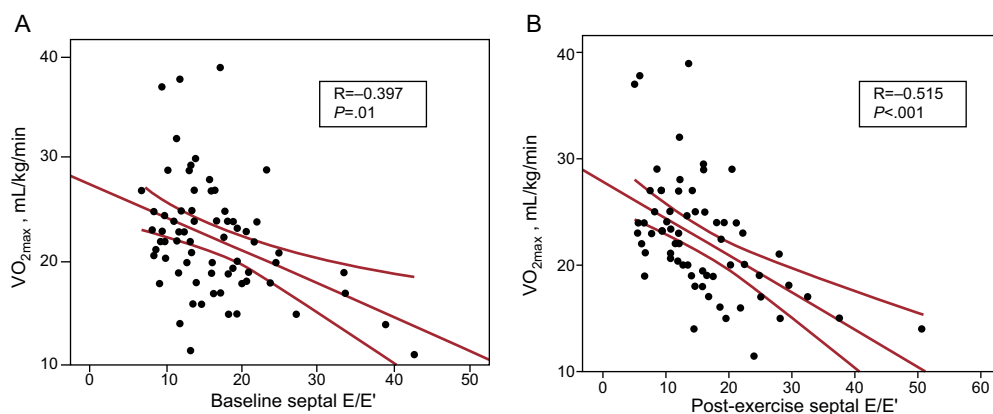


Figure 2. Simple correlation between oxygen consumption and septal E/E' ratio at rest (A) and after exercise (B). VO_{2max} , maximum oxygen consumption.

independent of the severity of obstruction. In effect, neither maximum at-rest gradient nor peak exercise gradient was significantly associated with VO_{2max} , even when we analyzed obstructive forms separately. Previous studies also failed to establish a relationship between gradient and functional limitation in these patients.^{4,22,23} Our study established the type of obstructive form based on Doppler study during exercise. In previous studies, the baseline or peak exercise gradients were assessed without considering the qualitative nature of the obstruction. We established the type of obstruction as an independent variable, since these obstructive forms not only involve a pressure gradient in the LVOT but are also associated with other mechanisms such as mitral regurgitation. In this manner, we observed that mitral regurgitation upon exercise was more common and severe in patients that suffered obstruction. As a consequence of these mechanisms, patients with obstruction have greater functional repercussions, both at rest and upon exercise. Thus, the left atrial volume, maximum wall thickness, and E/E' ratio, both at rest and during exercise, were significantly higher than in patients without obstruction. The fact that obstruction was one of the most important limiting factors is in accordance with previous studies in which a gradient >30 mmHg was a prognostic factor for heart failure and cardiovascular death.²⁴

Other factors associated with a greater functional limitation were age, left atrial volume, and Doppler parameters for E/A during exercise and the E/E' ratio of the septal ring. In our study, Doppler values obtained during peak exercise were better correlated with functional capacity (Fig. 2). When we only applied at-rest data in the predictive model, we obtained an $R^2=0.38$, whereas with the exercise data this value increased to 0.49. However, the results appear not to be quite clinically relevant, since a 50% variability rate seems excessive for predicting functional limitations in a given patient. This low predictive value of functional capacity in HCM patients is similar to the results published by other authors, whether using echocardiographic data,^{4,23,25,26} clinical data,²² or biological markers such as N-terminal pro-B-type natriuretic peptide.²⁷

During exercise, 14 patients had a pseudonormal pattern for mitral filling. We attributed this pseudonormalization, which was correlated with a lower VO_2 , to an increase in filling pressures during exercise. These patients have higher left atrial volumes, levels of mitral regurgitation, and E/E' ratios. Although the E/E' ratio in HCM patients does not reliably show LV pressure,¹⁵ upon exercising, as a consequence of increased heart rate, the shortening of diastole, and an increase in the preload due to mitral regurgitation, it is easy to understand that pressures increase in the presence of a hypertrophic and rigid LV. In a previous study, LV

stiffness, determined by a combination of Doppler ultrasound and cardiac magnetic resonance, was associated with a reduced functional capacity.²⁸

In patients without obstruction, LV volume was a determining factor for functional capacity. A higher ventricular volume was associated with a higher VO_2 . This coincides with the above-mentioned results, since a more dilated LV, with preserved LV ejection fraction, can maintain a higher cardiac output and higher VO_2 during exercise.

The indexed left atrial volume is the only echocardiographic variable that is independently associated with functional capacity in all patients, either with or without obstructions. Atrial remodelling reflects the chronicity and strong increase in atrial pressure. Atrial dilation has been associated with hypertrophy, diastolic dysfunction, increased filling pressures, reduced functional level, and increased risk of arrhythmia.²⁹ In clinical practice, indexed atrial volume is more useful than transverse diameter.³⁰ Our results coincide with previous studies (Table 5).³¹

Limitations

The analysis of the lateral ring was included halfway through the study, which is the reason why this variable was assessed in only 36 of the 87 patients. In the analysis of these 36 patients we did not observe that variables obtained from the lateral ring measurement improved compared to those of the septal ring, and it is not possible to conclude whether larger samples could improve the predictive value of these variables for functional capacity.

Table 5

Functional Capacity Values Expressed as Percentage of Maximum Oxygen Consumption. Multivariate Analysis

	All patients	Obstructions	No obstructions
Adjusted R^2	0.49	0.53	0.39
Age	0.002	0.003	0.025
LAVI	0.038	0.04	0.004
LVD	ns	ns	0.019
Obstruction	0.003		
Gradient	ns	ns	
E/E' after exercise	0.030	0.006	ns
E/A after exercise	0.001	0.014	ns

LAVI, left atrial volume index; LVD, left ventricular telediastolic volume; ns, not significant.

CONCLUSIONS

The Doppler ultrasound analysis during exercise facilitates recognition of latent obstruction and improves the predictive value for functional capacity over at-rest data, although it only explained 50% of the variability of this parameter. The type of obstruction is the most important independent factor for functional limitation. Additionally, age and left atrial volume are determining factors. E/A and E/E' ratios following exercise (in obstructed cases) and LV volume (in nonobstructed cases) were also independent factors associated with functional capacity.

CONFLICTS OF INTEREST

None declared.

REFERENCES

- Maron BJ. Hypertrophic cardiomyopathy. *Lancet*. 1997;350:127–33.
- Nishimura RA, Holmes Jr DR. Clinical practice: hypertrophic obstructive cardiomyopathy. *N Engl J Med*. 2004;350:1320–7.
- Matsumoto AY, Arteaga E, Ianni BM, Braga AM, Buck PC, Mady C. Relationships among exercise capacity, hypertrophy, and left ventricular diastolic function in nonobstructive hypertrophic cardiomyopathy. *Am Heart J*. 2005;150:144–9.
- Sharma S, Elliott P, Whyte G, Jones S, Mahon N, Whipp B, et al. Utility of cardiopulmonary exercise in the assessment of clinical determinants of functional capacity in hypertrophic cardiomyopathy. *Am J Cardiol*. 2000;86:162–8.
- Spirito P, Maron BJ. Relation between extent of left ventricular hypertrophy and diastolic filling abnormalities in hypertrophic cardiomyopathy. *J Am Coll Cardiol*. 1990;15:808–13.
- Shah JS, Esteban MT, Thaman R, Sharma R, Mist B, Pantazis A, et al. Prevalence of exercise-induced left ventricular outflow tract obstruction in symptomatic patients with non-obstructive hypertrophic cardiomyopathy. *Heart*. 2008;94:1288–94.
- Oh JK, Appleton CP, Hatle LK, Nishimura RA, Seward JB, Tajik AJ. The noninvasive assessment of left ventricular diastolic function with two-dimensional and Doppler echocardiography. *J Am Soc Echocardiogr*. 1997;10:246–70.
- Yu WC, Lee WS, Huang WP, Wu CC, Lin YP, Chen CH. Evaluation of cardiac function by tissue Doppler echocardiography: hemodynamic determinants and clinical application. *Ultrasound Med Biol*. 2005;31:23–30.
- Ommen SR, Nishimura RA, Appleton CP, Miller FA, Oh JK, Redfield MM, et al. Clinical utility of Doppler echocardiography and tissue Doppler imaging in the estimation of left ventricular filling pressures: a comparative simultaneous Doppler-catheterization study. *Circulation*. 2000;102:1788–94.
- Maron BJ, Spirito P, Green KJ, Wesley YE, Bonow RO, Arce J. Noninvasive assessment of left ventricular diastolic function by pulsed Doppler echocardiography in patients with hypertrophic cardiomyopathy. *J Am Coll Cardiol*. 1987;10:733–42.
- Nishimura RA, Appleton CP, Redfield MM, Ilstrup DM, Holmes Jr DR, Tajik AJ. Noninvasive Doppler echocardiographic evaluation of left ventricular filling pressures in patients with cardiomyopathies: a simultaneous Doppler echocardiographic and cardiac catheterization study. *J Am Coll Cardiol*. 1996;28:1226–33.
- Nihoyannopoulos P, Karatasakis G, Frenneaux M, McKenna WJ, Oakley CM. Diastolic function in hypertrophic cardiomyopathy: relation to exercise capacity. *J Am Coll Cardiol*. 1992;19:536–40.
- Pak PH, Maughan WL, Baughman KL, Kass DA. Marked discordance between dynamics and passive diastolic pressure-volume relations in idiopathic hypertrophic cardiomyopathy. *Circulation*. 1996;94:52–60.
- Nagueh SF, Lakkis NM, Middleton KJ, Spencer 3rd WH, Zoghbi WA, Quiñones MA. Doppler estimation of left ventricular filling pressures in patients with hypertrophic cardiomyopathy. *Circulation*. 1999;99:254–61.
- Geske JB, Sorajja P, Nishimura RA, Ommen SR. Evaluation of left ventricular filling pressures by Doppler echocardiography in patients with hypertrophic cardiomyopathy. Correlation with direct left atrial pressure measurement at cardiac catheterization. *Circulation*. 2007;116:2702–8.
- Report of the 1995 World Health Organization/International Society and Federation of Cardiology Task Force on the definition and classification of cardiomyopathies. *Circulation*. 1996;93:841–2.
- Schiller NB, Shah PM, Crawford M, DeMaria A, Devereux R, Feigenbaum H, et al. Recommendations for quantitation of the left ventricle by two-dimensional echocardiography. American Society of Echocardiography Committee on Standards, Subcommittee on Quantitation of Two-Dimensional Echocardiograms. *J Am Soc Echocardiogr*. 1989;2:358–67.
- García MJ, Thomas JD, Klein AL. New Doppler echocardiographic applications for the study of diastolic function. *J Am Coll Cardiol*. 1998;32:865–7.
- Lang RM, Bierig M, Devereux RB, Flachskampf FA, Foster E, Pellikka PA, et al.; Chamber Quantification Writing Group. American Society of Echocardiography's Guidelines and Standards Committee; European Association of Echocardiography, Recommendations for chamber quantification: a report from the American Society of Echocardiography's Guidelines and Standards Committee and the Chamber Quantification Writing Group, developed in conjunction with the European Association of Echocardiography, a branch of the European Society of Cardiology. *J Am Soc Echocardiogr*. 2005;18:1440–63.
- Wasserman K, Van Kessel AL, Burton GG. Interaction of physiological mechanisms during exercise. *J Appl Physiol*. 1967;22:71–85.
- Elliott PM, Poloniecki J, Dickie S, Sharma S, Monserrat L, Varnava A, et al. Sudden death in hypertrophic cardiomyopathy: identification of high risk patients. *J Am Coll Cardiol*. 2000;36:2212–8.
- De la Morena-Valenzuela G, Florenciano-Sánchez R, García-Almagro FJ, González-Caballero E, Pascual-Figal D, Soria-Arcos F, et al. Evaluación funcional de los pacientes con miocardiopatía hipertrófica mediante análisis del consumo de oxígeno máximo. *Rev Esp Cardiol*. 2003;56:865–72.
- Le VV, Perez MV, Wheeler MT, Myers J, Schnittger I, Ashley EA. Mechanisms of exercise intolerance in patients with hypertrophic cardiomyopathy. *Am Heart J*. 2009;158:e27–34.
- Olivetto I, Maron BJ, Monterege A, Mazzuoli F, Dolara A, Cecchi F. Prognostic value of systemic blood pressure response during exercise in a community-based patient population with hypertrophic cardiomyopathy. *J Am Coll Cardiol*. 1999;33:2044–51.
- Ha JW, Ahn JA, Kim JM, Choi EY, Kang SM, Rim SJ, et al. Abnormal longitudinal myocardial functional reserve assessed by exercise tissue Doppler echocardiography in patients with hypertrophic cardiomyopathy. *J Am Soc Echocardiogr*. 2006;19:1314–9.
- Matsumura Y, Elliott PM, Virdee MS, Sorajja P, Doi Y, McKenna WJ. Left ventricular diastolic function assessed using Doppler tissue imaging in patients with hypertrophic cardiomyopathy: relation to symptoms and exercise capacity. *Heart*. 2002;87:247–51.
- Thaman R, Esteban MT, Barnes S, Gimeno JR, Mist B, Murphy R, et al. Usefulness of N-terminal pro-B-type natriuretic peptide levels to predict exercise capacity in hypertrophic cardiomyopathy. *Am J Cardiol*. 2006;98:515–9.
- Dumont CA, Monserrat L, Peteiro J, Soler R, Rodríguez E, Bouzas A, et al. Relation of left ventricular chamber stiffness at rest to exercise capacity in hypertrophic cardiomyopathy. *Am J Cardiol*. 2007;99:1454–7.
- Yang H, Woo A, Monakier D, Jamorski M, Fedwick K, Wigle ED, et al. Enlarged left atrial volume in hypertrophic cardiomyopathy: a marker for disease severity. *J Am Soc Echocardiogr*. 2005;18:1074–82.
- Khankirawatana B, Khankirawatana S, Porter T. How should left atrial size be reported? Comparative assessment with use of multiple echocardiographic methods. *Am Heart J*. 2004;147:369–74.
- Saura D, Marín F, Climent V, González J, Roldán V, Hernández-Romero D, et al. Left atrial remodelling in hypertrophic cardiomyopathy: relation with exercise capacity and biochemical markers of tissue strain and remodelling. *Int J Clin Pract*. 2009;63:1465–71.