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Original article

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

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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/m^2 vs 31.1 [11.6] mL/m^2; *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 R^2 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.

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

Palabras clave:
Miocardiopatía hipertrófica
Ecocardiografía de estrés
Consumo de oxígeno

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 ± 5,7 frente a 24,6 ± 6,1 ml/kg/min; p = 0,012), presentaban mayor volumen auricular izquierdo (42,1 ± 14,5 frente a 31,1 ± 11,6 ml/m^2; 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 (R^2 ajustada = 0,49 frente a R^2 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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Abbreviations

HCM: hypertrophic cardiomyopathy
LV: left ventricle
LVOT: left ventricular outflow tract
VO_2: 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 (VO_2) 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 $\leq$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$>$30 mmHg in the stress test. The classification of mitral regurgitation was based on the planar analysis of the regurgitating surface: mild (1-4 cm^2), moderate (4-8 cm^2), and severe ($>$8 cm^2). Left atrial volume indexed for body surface area was obtained using the 2-plane Simpson method (mL/m^2).[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 VO_2, VCO_2, 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$\leq$0.85. VO_{2max} was established as the highest value of the 10-s averages during the last minute of exercise (in mL/kg/min). Functional capacity was determined as the percentage of the observed maximum VO_{2max} as compared to the theoretical maximum value based on age, sex, and body surface area.[20] The criteria for interrupting the test were exhaustion, severe arrhythmia, severe hypertension (systolic$>$240 mmHg or diastolic$>$110 mmHg), hypotensive response ($>$20 mmHg), or limiting symptoms. We defined an abnormal pressure response as an increase$<$25 mmHg or a drop$>$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