Dynamic Left Ventricular Outflow Tract Obstruction Induced by Exercise

Fernando Cabrera Bueno, Isabel Rodríguez Bailón, Raúl López Salguero, Juan J. Gómez Doblas, Alejandro Pérez Cabeza, José Peña Hernández, Antonio Domínguez Franco, Luis Morcillo Hidalgo, and Eduardo de Teresa Galván

Servicio de Cardiología, Hospital Universitario Virgen de la Victoria, Málaga, Spain.

Introduction and objectives. Dynamic left intraventricular outflow tract obstruction occurs occasionally in patients without hypertrophic cardiomyopathy. We hypothesized that dynamic intraventricular obstruction might occur during effort in patients with angina or dyspnea without evident disease. The objective of this prospective study was to investigate: *a)* whether it appears with effort; *b)* its incidence, magnitude and determining factors; and *c)* its clinical course.

Patients and method. We performed baseline and stress Doppler echocardiography in 211 patients with angina, dyspnea, or both with exercise. Patients with previous myocardial infarction, valvular heart disease, ventricular dysfunction or ventricular hypertrophy without hypertension were excluded. Dynamic intraventricular obstruction was defined as intracavitary flow velocity ≥2.5 m/s.

Results. 134 patients (59 women) were included: mean age was 58 (9) years; history of hypertension was present in 69.7%, dyslipidemia in 35.8%, and diabetes in 24.6%. Dynamic intraventricular obstruction appeared in 18 patients (13.4%), with gradients ranging between 25 and 53 mm Hg (mean, 32.19 [6.6]). Demographic variables, cardiovascular risk factors, and exercise performed were similar in group A (with obstruction) and group B (without obstruction). No patient in group A had evidence of ischemia. Five patients in this group had symptoms during exercise; the gradients were greater in these patients (42.65 [10.5] vs 28.15 [2.37] mm Hg; *P*<.0001) than in the remaining group A patients. Left ventricular outflow tract size was found to be the only independent predictive factor in the multivariate analysis. After 369.9 (133.5) days of follow-up, no cardiac events were recorded.

Conclusions. Our study suggests that some patients with angina or dyspnea without evidence of ischemia may develop dynamic left ventricular outflow tract obstruction induced by effort.

Key words: *Obstruction. Exercise. Ventricular.*

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Correspondence: Dr. F. Cabrera Bueno.
Madame Bovary, 21, casa 14. 29620 Torremolinos. Málaga. España.
E-mail: fonendo@hotmail.es

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Obstrucción dinámica intraventricular izquierda inducida por esfuerzo

Introducción y objetivos. La obstrucción dinámica intraventricular izquierda puede aparecer ocasionalmente en pacientes sin miocardiopatía hipertrófica. Planteamos si podría aparecer inducida por esfuerzo en pacientes con angina o disnea de esfuerzo sin causa aparente. El objetivo de este estudio prospectivo es conocer: *a)* si aparece con esfuerzo; *b)* su incidencia, magnitud y factores determinantes, y *c)* evolución de los pacientes que la presentan.

Pacientes y método. Realizamos ecocardiograma-Doppler basal y postesfuerzo en 211 pacientes con angina o disnea de esfuerzo. Excluimos a los que tenían infarto previo, valvulopatía, disfunción ventricular o hipertrofia ventricular sin hipertensión. Definimos obstrucción dinámica intraventricular como flujo intraventricular con velocidad ≥ 2,5 m/s.

Resultados. Se incluyó a 134 pacientes (59 mujeres), con una edad de 58 ± 9 años; el 69,7% tenía antecedentes de hipertensión, el 35%, dislipemia y el 24,6%, diabetes. Apareció obstrucción intraventricular en 18 (13,4%) pacientes, con un gradiente entre 25 y 53 mmHg (media, 32,19 ± 6,6). Las variables demográficas, los factores de riesgo y el ejercicio realizado fueron similares en el grupo A (con obstrucción) y B (sin obstrucción). En el grupo A, ningún paciente tuvo evidencia de isquemia y los 5 que presentaron síntomas durante el esfuerzo tuvieron mayores gradientes (42,65 ± 10,5 frente a 28,15 ± 2,37 mmHg; p < 0,0001) que el resto del grupo A. El análisis multivariante identificó el diámetro del tracto de salida como único factor predictor independiente. Tras un seguimiento de 369,9 ± 133,5 días, no se registraron eventos.

Conclusiones. Nuestros datos sugieren que algunos pacientes con angina o disnea de esfuerzo sin evidencia de isquemia pueden tener obstrucción dinámica ventricular izquierda inducida por esfuerzo.

Palabras clave: *Obstrucción. Esfuerzo. Ventricular.*

ABBREVIATIONS

DLVOTO: dynamic left ventricular outflow tract obstruction.

INTRODUCTION

Dynamic left ventricular outflow tract obstruction (DLVOTO) is a common observation in hypertrophic cardiomyopathy. Nevertheless, it has also been reported under other circumstances such as dobutamine administration,[1] postoperative period for mitral,[2] or aortic[3,4] valve surgery, or acute coronary syndromes.[5-7] Dobutamine-induced DLVOTO was described by Pellikka[1] in 1992 as a phenomenon that appears in 21% of dobutamine echocardiograms. Later, its appearance has been related to unexplained chest pain in patients with normal echocardiogram at rest,[8] to angina in patients with normal coronary angiogram,[9] and to exertional dyspnea in elderly patients.[10] It has also been suggested that its appearance could be improved or eliminated with beta-blockers,[11] although its clinical and prognostic significance has not been definitively established.

The fact that DLVOTO appears in some patients during dobutamine echocardiography suggests that it might also appear during exercise. However, the observation of this phenomenon during exercise has been reported in the literature only a few times,[12-14] and thus the factors related to its appearance and its potential clinical significance have not been established. Exercise- or stress-induced dynamic obstruction that disappears upon rest could produce symptoms, with these symptoms hard to explain in hearts with little or no structural abnormalities. If this hypothesis is verified, it could identify a possible cause of angina or dyspnea in patients without evidence of cardiomyopathy or coronary disease, leading to therapy based on negative inotropic drugs. Hence, this study was undertaken with the following objectives:

1. To perform a prospective study on the possible appearance of DLVOTO during exercise.

2. To determine its incidence and extent, and the factors related to its appearance.

3. To analyze the clinical progress of patients with this condition.

PATIENTS AND METHODS

Patients

Two hundred and eleven consecutive patients referred for stress testing were studied; 134 of these patients met the following inclusion criteria:

1. Clinical symptoms of dyspnea or chest pain with an intermediate probability of coronary disease.

2. Possibility to perform stress echocardiography with adequate technical quality.

3. Completion of exercise until the submaximal heart rate was exceeded or presenting evidence of ischemia.

4. Sinus rhythm.

Patients with the following were excluded: *a)* known history of coronary disease (myocardial infarction or documented ischemia); *b)* overall or regional contractility alterations in the baseline tracing; *c)* moderate to severe valvular disease; *d)* left ventricular hypertrophy with no history of hypertension; and *e)* presence of dynamic subaortic obstruction to any degree in the baseline echocardiogram or family history of hypertrophic cardiomyopathy.

Stress Echocardiography

All patients were tested following the Bruce treadmill protocol after 4 h of fasting and discontinuation of anti-ischemic drugs for the previous 72 h. The test was considered valid if the submaximal heart rate was exceeded or evidence of myocardial ischemia appeared, with the latter defined as a horizontal or descending ST-segment depression greater than 0.1 mV at 80 milliseconds after the J point in the electrocardiogram.

The echocardiographic examination was performed using a VingMed ultrasound machine equipped with Super-VHS recording system and Pinnacle DV500 Plus system, using a 2.5-3.25 MHz probe. Baseline 2-dimensional M-mode echocardiography images were obtained by color and spectral Doppler ultrasound. Left ventricular outflow tract diameter was measured in the longitudinal plane during systole as the shorter distance between the anterior mitral valve and the interventricular septum. Immediately after exercise (60-120 s), echocardiographic images were acquired with the patient in lateral decubitus, starting with ventricular flow.

M-mode echocardiographic measurements of the left ventricle were taken in accordance with the recommendations of the American Society of Echocardiography (ASE),[15] and left ventricular mass was calculated according to the modified Devereux formula[16] for the ASE standards:

$$LVmass=0.80\{1.04[IVSTd+PWTd+LVIDd]^3-LVIDd^3\}+0.6\ g$$

where LV is the left ventricle; IVSTd, intraventricular septal thickness at end-diastole; PWT, posterior wall thickness at end-diastole; and LVIDd, left ventricular internal dimension at diastole.

Both the dimensions and the mass are expressed as indexed to body surface area.

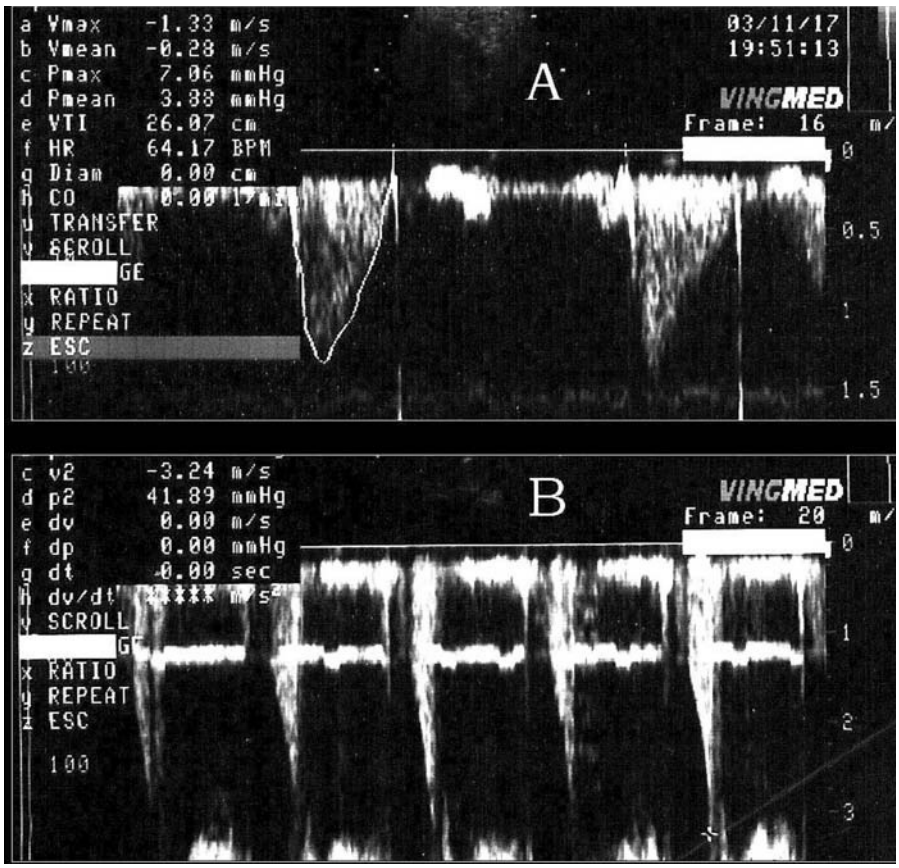

Figure 1. Continuous Doppler recordings of left ventricular outflow tract velocity, obtained at rest (A) and immediately post-exercise (B).

Hypertrophy was considered to exist when the left ventricular mass index was above 125 g/m^2, in accordance with studies identifying this as an effective cutoff to predict cardiovascular events.[17,18]

Left ventricular geometry was also assessed by calculating the relative wall thickness from the following formula:

$$RWT=IVSTd+PWTd/LVIDd$$

Based on a relative wall thickness >0.45 and the presence or absence of hypertrophy, patients were classified as having one of 4 types of ventricular geometry with prognostic significance:[18,19] normal, concentric hypertrophy, eccentric hypertrophy, and concentric remodeling; the possible relation between type of ventricular geometry and appearance of exercise-induced DLVOTO was then analyzed.

Follow-up

Follow-up consisted of a medical history review or phone interview with the patients or their relatives to identify cardiovascular events such as death, myocardial infarction, unstable angina, heart failure, documented arrhythmia, or syncope.

Definition of Transient Dynamic Left Ventricular Outflow Tract Obstruction

As established in other publications,[4,20] DLVOTO was defined as the presence of systolic flow at a velocity equal to or greater than 2.5 m/s (equivalent to 25 mm Hg) and dagger-shaped late peaking in the left ventricular outflow tract or mid-ventricular region not present at baseline and disappearing after the recovery phase (Figure 1).

Statistical Analysis

Continuous variables are expressed as mean ± standard deviation, and qualitative variables as percentages. The variables analyzed were compared in 2 groups according to the appearance of DLVOTO or not. The Chi-square test was used for qualitative variables, and one-way analysis of variance for continuous variables. Significance was set at a *P*-value <.05. Multivariate analysis was also performed using a multiple logistic regression model to identify independent predictive variables of the appearance of DLVOTO, with this model including those variables which reached a significance level below 0.1 in the univariate analysis. The odds ratio (OR) and 95% confidence intervals

(CI) were calculated from the parameters estimated by the regression model. SPSS for Windows was used for the statistical analysis.

RESULTS

General and Clinical Data for the Patients

A total of 134 patients (59 women, 75 men) with a mean age of 58±9 years (range, 37 to 76 years) were included; 69.4% had hypertension; 35.8%, dyslipidemia; 9%, active smoker, and 24.6%, diabetes mellitus.

Symptoms were chest pain in 67.9% of the patients and exertional dyspnea in 32.1%; the mean functional class was 1.71±0.60.

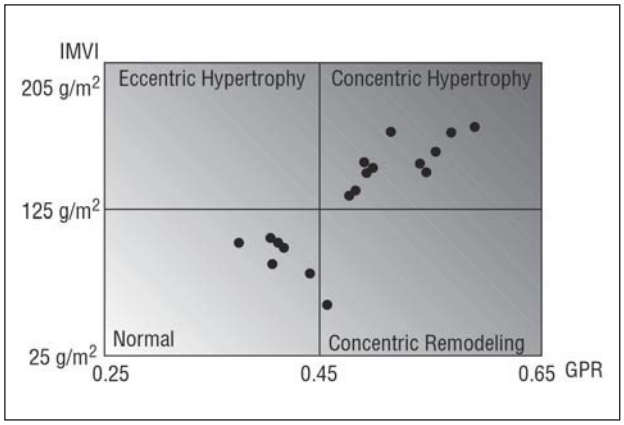

Figure 2. Distribution of patients with dynamic left ventricular outflow tract obstruction, according to ventricular morphology. RWT indicates relative wall thickness; LVMI, left ventricular mass index.

Effort-Related Data

Post-exercise echocardiogram detected DLVOTO in 18 (13.4%) patients, with a gradient of 25 to 53 mm Hg (mean, 32.19±6.63 mm Hg), that disappeared in the following minutes during the recovery phase. These patients were considered group A, and the 116 remaining patients, group B.

A comparative analysis of the demographic and clinical variables (Table 1) showed that both groups were similar except in the functional class, which was higher in group A. The behavior of both groups during the exercise was similar (Table 2). A comparison of the echocardiographic variables (Table 3) showed that the patients of group A had greater wall thickness and smaller outflow tract and ventricular chamber diameters. In contrast, the ratio of septal to posterior wall thickness and the parameters of systolic and diastolic function were similar in both groups. In terms of ventricular geometry, group A was more likely to present concentric hypertrophy (61.1% vs 18.96%; *P*=.045), although some patients in this group had normal geometry (Figure 2).

The post-exercise echocardiogram showed a similar

TABLE 1. **Statistical Analysis: Clinical Variables***

Patients (n=134)	Group A, Patients With DLVOTO (n=18)	Group B, Patients Without DLVOTO (n=116)	*P*
Age, years	56.78±9.21	59.08±9.0	.316
Sex, female	13 (72.2%)	62 (53.4%)	.107
Weight, kg	82.18±14.43	77.38±11.79	.133
Height, cm	163.65±9.24	162.14±9.76	.522
BSA	1.86±0.16	1.81±0.16	.178
Cardiovascular risk factors			
Hypertension	15 (83.33%)	78 (67.24%)	.133
Dyslipidemia	7 (38.88%)	41 (35.34%)	.492
Smoking	3 (16.66%)	9 (7.75%)	.068
Diabetes mellitus	4 (22.22%)	29 (25%)	.523
Clinical condition			
Dyspnea	8 (44.44%)	35 (30.17%)	.174
Chest pain	17 (94.44%)	95 (81.89%)	.160
Functional class	2.22±0.43	1.63±0.58	.000[a]
Treatment			
Beta-blockers	3 (16.66%)	51 (43.96%)	.017[a]
Calcium antagonists	7 (38.88%)	33 (28.44%)	.266
Nitrates	2 (11.11%)	15 (12.93%)	.585
ACE inhibitors/ARBs	6 (33.33%)	30 (25.86%)	.350
Diuretics	5 (27.77%)	7 (6.03%)	.011[a]

*ACE inhibitors indicates angiotensin-converting enzyme inhibitors; ARBs, angiotensin II receptor blockers; BSA, body surface area; DLVOTO, dynamic left ventricular outflow tract obstruction.
[a]*P*<.05.

TABLE 2. **Exercise-Related Variables***

	Group A, Patients With DLVOTO (n=18)	Group B, Patients Without DLVOTO (n=116)	*P*
Baseline parameters			
Systolic BP, mm Hg	144.17±23.53	142.93±21.20	.821
Diastolic BP, mm Hg	80.28±10.50	80.26±9.80	.994
Heart rate, bpm	88±14.44	81.41±15.04	.063
Post-exercise parameters			
Systolic BP, mm Hg	180.28±28.52	170.91±24.09	.821
Systolic BP change, %	26.86±23.80	20.70±16.27	.168
Diastolic BP, mm Hg	87.22±10.60	84.31±11.48	.994
Diastolic BP change, %	10.00±18.24	5.50±11.89	.171
Heart rate, bpm	144.83±29.44	143.39±26.40	.344
Exercise time	6'14''±2'26''	6'47''±2'10''	.329
Theoretical MHR, %	95.06±11.04	90.78±11.77	.155
Double product	27311.11±7431.86	24489.74±5576.50	.059
Work, METs	7.89±2.33	8.31±2.27	.465
Interpretation			
Electrically positive	0	17 (14.65%)	.072
Clinically positive	5 (27.77%)	14 (12.06%)	.085

*BP indicates blood pressure; DLVOTO, dynamic left ventricular outflow tract obstruction; MHR, maximum heart rate achieved.

TABLE 3. **Statistical Analysis: Echocardiographic Variables***

	Group A, Patients With DLVOTO (n=18)	Group B, Patients Without DLVOTO (n=116)	*P*
Baseline parameters			
LVEDDi, mm/m^2	25.02±2.39	27.00±2.57	.003
LVESDi, mm/m^2	15.65±2.28	17.37±3.03	.024
Septumi, mm/m^2	5.96±1.12	5.40±1.01	.035
Posterior wall thickness index, mm/m^2	5.94±1.08	5.39±0.89	.022
Ratio of septal to posterior wall thickness	1.00±0.09	1.00±0.09	.942
LVOT diameteri, mm/m^2	8.47±0.90	9.95±0.88	.024
Ejection fraction, %	73.00±6.67	69.58±8.71	.113
Shortening fraction, %	36.76±5.87	35.46±5.61	.372
V_{max}, Ao, m/s	1.38±0.27	1.15±0.24	.001
TVI Ao, cm	25.44±6.08	23.43±5.76	.214
V_{max}, E, m/s	0.85±0.19	0.82±0.19	.629
V_{max}, A, m/s	0.87±0.20	0.81±0.19	.280
E:A ratio	0.99±0.21	1.04±0.30	.531
E:A ratio <1	7 (38.80%)	42 (36.20%)	.597
LVH	11 (61.11%)	32 (27.58%)	.006
LV mass index, g/m^2	129.77±37.03	111.45±30.57	.025
RWT	0.47±0.07	0.40±0.06	.000
RWT>0.45	12 (66.66%)	6 (5.17%)	.000
LVH+RWT >0.45	11 (61.11%)	22 (18.96%)	.045
Post-exercise parameters			
Ejection fraction	75.22±63	73.42±7.31	.827
Maximum velocity, m/s	2.78±0.34	1.63±0.34	.000
LVEDDi, mm/m^2	24.62±2.00	26.49±2.51	.018
LVESDi, mm/m^2	14.73±205	15.55±2.23	.215
Ischemia data	0	7 (6.03%)	.355
Appearance of SAM	1 (5.55%)	0	.134
Appearance of MR	1 (5.55%)	1 (0.8%)	.251

*$LVEDD_i$ indicates left ventricular end-diastolic diameter index; $LVESD_i$, left ventricular end-systolic diameter index; Septumi, septal thickness index; RWT, relative wall thickness; LVH, left ventricular hypertrophy; TVI Ao, time-velocity integral of aortic flow; DLVOTO, dynamic left ventricular outflow tract obstruction; MR, mitral regurgitation; SAM, systolic anterior motion of the mitral valve; LVOT diameteri, left ventricular outflow tract diameter index; V_{max}, maximum velocity.

TABLE 4. **Examination Results for the 18 Patients With Coronary Angiography***

Patient	Group	Clinical Ergometry	Ergometry-ECG	Baseline Echo	Exercise Echo	Exercise Scintigraphy	Coronary Angiography
1	A	$+^{S2}$	–	LVH	DLVOTO	RPD (inferior)	Normal (milking effect in LAD)
2	A	$+^{S2}$	–	Normal	DLVOTO	RPD (anterior)	Normal
3	B	$+^{S2}$	$+^{S2}$	Normal	Normal		Normal
4	B	–	$+^{S2}$	LVH	IP isch.		90% pRCA (stent)
5	B	$+^{S2}$	$+^{S2}$	Normal	Normal		Normal
6	B	$+^{S2}$	–	LVH	Apic. isch.	RPD (anterior)	90% pLAD (stent)
7	B	–	$+^{S2}$	Normal	Normal	RPD (anterior)	Normal-dissection-stent
8	B	$+^{S3}$	$+^{S2}$	Normal	Ant. isch.		Triple-vessel disease (surg.)
9	B	–	$+^{S2}$	Normal	Post. isch.		90% pRCA (stent)
10	B	–	$+^{S2}$	LVH	IPL isch.		Triple-vessel disease (stent)
11	B	$+^{S2}$	$+^{S2}$	LVH	Normal		Normal
12	B	–	$+^{S1}$	Normal	Ant. isch.		Triple-vessel and LCA disease (surg.)
13	B	–	$+^{S2}$	Normal	Normal		Normal
14	B	–	$+^{S2}$	Normal	Normal		Normal
15	B	$+^{S2}$	$+^{S2}$	LVH	Normal		Normal
16	B	–	$+^{S2}$	LVH	Normal		Normal
17	B	–	$+^{S2}$	Normal	Ant. isch.		Triple-vessel and LCA disease (surg.)
18[a]	B	–	–	LVH	Normal	Normal	90% pRCA

*pRCA indicates proximal right coronary artery; pLAD, proximal left anterior descending artery; RPD, reversible perfusion defect; LVH, left ventricular hypertrophy; Ant. isch., anterior ischemia; Apic. isch., apical ischemia; IP isch., inferoposterior ischemia; IPL isch., inferior and posterolateral ischemia; DLVOTO, dynamic left ventricular outflow tract obstruction; LCA, left coronary artery; Surg.: surgical treatment; $+^{Sx}$, stage of positivity; –, negative.
[a]Coronary angiography performed 6 months later for unstable angina.

ejection fraction for both groups. No patients in group A presented ischemia data, versus 6.03% in group B who did. In group A, 5 (27.7%) patients had precordial oppression during exercise that was identified as their usual symptoms. No patient presented alterations in the electrocardiogram or a disproportionate elevation of blood pressure. In 4 patients, the myocardial scintigraphy was normal; the remaining case had a perfusion defect, but the coronary angiography was normal. In 1 patient, mitral regurgitation with exertion was detected, along with systolic anterior motion of the mitral valve. These 5 patients presented significantly higher exercise-induced gradients (42.65±10.5 mm Hg vs 28.15±2.37 mm Hg; $P<.0001$) than the rest of the group A patients with no symptoms during exercise.

In group B, 7 patients presented disturbances in regional contractility, with transient mitral regurgitation accompanied by inferoposterior hypokinesia in one of them.

Multivariate Analysis

A logistic regression model was constructed with the following variables: functional class, prior treatment, ventricular and outflow tract diameter, septal and posterior wall thickness, ratio of septal to posterior wall thickness, left ventricular hypertrophy, relative wall thickness, heart rate, and maximum outflow tract velocity at baseline. The only independent predictive factor of the appearance of DLVOTO during the post-exercise period was outflow tract diameter, measured in the baseline echocardiogram and adjusted to body surface area ($P<.0001$), with an OR of 0.092 (0.029-0.275) for 95% CI.

Usefulness of Outflow Tract Diameter as a Predictive Parameter of Exercise-Induced DLVOTO

Considering the left ventricular outflow tract 9.25 cm/m^2 as a predictor of exercise-induced DLVOTO, this parameter presents a sensitivity of 94%, a specificity of 82% and a positive predictive value of 45.9%. In contrast, a value above 9.25 cm/m^2 has a negative predictive value of 98.9%.

Clinical Follow-up Data

Data on clinical progress were obtained for 131 (97.7%) of the 134 patients, with a mean time of 369.9±133.5 days (range, 172-722 days). Among the 3 patients lost in follow-up, 1 belonged to group A and the other 2, group B.

No events were recorded in group A; 2 patients who had presented with angina and a perfusion defect on exercise scintigraphy underwent coronary angiography, with normal results in both cases.

In group B, 1 episode of unstable angina was reported 6 months after the initial study, which had been negative, and the coronary angiography showed a single 90% lesion in the posterior descending artery. Based on the initial study results, another 15 patients from this group underwent a scheduled coronary angiography; significant lesions (stenosis, 50% in the left

coronary and 70% in the rest of the epicardial coronary vessels) were found in 7 cases.

The findings in patients who underwent coronary angiography and the respective additional non-invasive examinations are shown in Table 4, indicating that 5 patients in group B could be classified as carriers of cardiac syndrome X, since they presented exertional angina, electrocardiographic abnormalities suggestive of ischemia, and normal coronary angiography.

DISCUSSION

In this prospective series of patients with an increased prevalence of hypertension and clinical symptoms of chest pain or exertional dyspnea with normal systolic function, DLVOTO was induced by exercise in 13.4% of the cases. This incidence is higher than the 1.7% reported by Peteiro et al[12] for a variety of potential reasons. First of all, the characteristics of the study population differed. In the Peteiro series all patients underwent stress echocardiography, whereas our study excluded patients with proven coronary disease or ventricular dysfunction, significant valve disease, or ventricular hypertrophy in the absence of hypertension or insufficient exercise. Secondly, ventricular flow velocities were measured immediately after exercise in our patients and not after analyzing regional contractility, which could have contributed to recording a larger number of gradients, given the tendency for the gradient to disappear in the minutes after exercise. In a recent PubMed search, we found only four other publications[13,14,21,22] related to exercise-induced intraventricular gradient in patients without hypertrophic cardiomyopathy. Two of them describe patients who showed DLVOTO during dobutamine echocardiography but not during exercise although the low number of cases (15 in one[14] and 10 in the other[21]) make it impossible to draw definitive conclusions. In the third publication, Meimoun et al[22] present 2 patients with exertional dyspnea of no apparent cause who showed DLVOTO with SAM of the mitral valve and mitral regurgitation in the dobutamine echocardiography. In both cases DLVOTO together with dyspnea reappeared in the stress echocardiography. In the last paper, Cotrim et al[13] describe a similar condition in a young man.

The univariate analysis identified hypertrophy, particularly the concentric type (relative wall thickness >0.45), as a predictor of exercise-induced DLVOTO. This is consistent with the findings of Harrison et al[23] in 1991, in which some elderly patients with hypertension and severe concentric hypertrophy presented had an mid-ventricular obstruction in the Doppler echocardiogram at rest. It seems paradoxical that the group with a higher incidence of hypertrophy secondary to hypertension had a lower incidence of coronary disease; this is attributable to the sample size and the higher frequency of other risk factors in the group without DLVOTO.

Asymmetric hypertrophy with septal predominance was not a predictive factor for obstruction in our series. This could be due to the low number of patients with this condition among our study population.

In the multivariate analysis, the only predictive factor for DLVOTO was left ventricular outflow tract diameter as measured in the baseline echocardiogram. We found that a value ≤9.25 mm/m^2 can predict exercise-induced DLVOTO with a sensitivity of 94%, a specificity of 82% and a positive predictive value of only 45.9%. In contrast, a value above 9.25 mm/m^2 has a negative predictive value of 98.9%. A simple measurement in the conventional resting echocardiogram could rule out the possible appearance of obstruction.

The clinical significance of DLVOTO in the absence of hypertrophic cardiomyopathy is still under debate in the literature. In our series, a linear relationship could not be established between the appearance of a pressure gradient and the patient's symptoms. This is the result of several factors. First of all, the stress tests were not performed to reproduce symptoms, but to find evidence of ischemia, since this was the reason why the patients consulted. Secondly, left ventricular flow was recorded immediately after rather than during exercise; hence, the extent of the gradient might have been underestimated because it disappears quickly during the recovery phase. In addition, the decubitus position in which the measurements were taken could also contribute to decreasing the gradient due to the preload increase involved in lying down.

The percentage of group A patients with angina-like symptoms during the stress test was not very high (27.7%), although the gradients were significantly higher in this subgroup (42.65±10.5 mm Hg vs 28.15±2.37 mm Hg; P<.0001) than in the rest of the group A patients.

The patients with DLVOTO showed no exercise-related electrocardiographic abnormalities, and therefore syndrome X[24] can be ruled out as a cause of their symptoms. Conversely, group B had 5 patients (3.7% of all patients studied for angina or exertional dyspnea) who could be classified as carriers of this syndrome and had findings consistent with the description by Zouridakis et al,[25] as the stress echocardiogram did not detect ischemia in syndrome X patients.

We did not observe any episode of transient apical ballooning syndrome,[26-28] which some authors, such as Penas-Lado et al[29] and Barriales Villa et al,[30] consider may be secondary to the appearance of a transient dynamic intraventricular gradient in situations of severe adrenergic stimulation or hypovolemia. However, other authors[28] have related it to vasospasm, microcirculation disturbances, or an unusual anatomy of the left anterior descending artery.[31] Longer follow-up of our patients might indicate whether or not their capacity to present DLVOTO makes them more likely to

develop transient apical ballooning.

Patients who presented exercise-induced DLVOTO in our series had a good prognosis at mid-term, as no events were observed after a mean follow-up of one year. This is consistent with the progress described by Barletta et al[20] in patients with dobutamine-induced DLVOTO, but contrasts with the adverse prognosis described for DLVOTO appearing postoperatively[32,33] or in acute coronary syndromes,[5,34-36] in which the use of inotropic drugs or vasodilators can worsen the obstruction or hemodynamic deterioration.

Limitations

In this study, flow velocities and intraventricular gradient were measured immediately after exercise, rather than during maximal exercise. This is inevitable with treadmill testing, but may mean a lower gradient measurement, as the gradient tends to decrease only a few minutes after exercise is stopped. Moreover, the echocardiogram was recorded while the patient was lying down, making it easier to obtain the images, but possibly contributing to decreasing the gradient by increasing venous return and preload.

Another limitation is the absence of any relation between gradient induction and the reproduction of symptoms in some patients. Among other reasons, this may be because the exercise was done to detect evidence of ischemia or to exceed the submaximal heart rate, rather than to reproduce the symptoms. In order to analyze this relationship, it would be necessary to do the comparison with a control group of symptom-free subjects having demographic characteristics similar to those of the patients.

Clinical Implications

The data from this study suggest that in the absence of hypertrophic cardiomyopathy, DLVOTO can be induced by exercise in some patients with angina or exertional dyspnea and no evidence of ischemia, and this could be the cause of their symptoms. More studies are needed to confirm this finding and to determine the response of these patients to negative inotropic treatment. If confirmed, transient DLVOTO would have to be considered another cause of angina with normal coronary angiography.

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