Predictors of Myocardial Contractile Reserve in Patients With Nonischemic Dilated Cardiomyopathy. An Echo-Stress Dobutamine Study

Matías Pérez-Paredes, Andrés Carnero, Diego M. Giménez, José A. Ruiz Ros, Manuel Gonzálvez, Andrés Carrillo, María J. Cascales, Francisco Martínez-Corbalán, María J.G. Villalba, and Tomás Cubero

Unidad de Cardiología, Laboratorio de Ecocardiografía, Hospital Universitario Morales Meseguer, Murcia, Spain.

Introduction and objectives. Myocardial contractile reserve studies with low-dose dobutamine echocardiography have been shown to be useful to assess functional myocardial status. However, the variables associated with contractile reserve after inotropic stimulation are not well known.

Patients and method. We studied 50 patients (35 men, mean age 56.4 ± 9.5 years) with nonischemic dilated cardiomyopathy (NIDC), LVEF 28.7% ± 8.5% and wall motion score index (WMSI) 2.42 ± 0.34 with low-dose dobutamine echocardiography. Left ventricular contractile reserve was assessed by a differential parameter defined as the difference between rest and stress WMSI (ΔWMSI).

Results. After dobutamine infusion the WMSI was 1.95 ± 0.58; from this value we calculated a ΔWMSI of 0.45 ± 0.39. None of the clinical variables showed a relationship with the presence of contractile reserve. In contrast, the following echocardiographic parameters correlated with ΔWMSI: end-diastolic (p = 0.05) and end-systolic (p = 0.02) diameters, end-systolic volume index (p = 0.01) and LVEF (p = 0.002). In the multivariate analysis, only end-diastolic diameter was an independent predictor of contractile reserve (hazard ratio = 0.852; 95% CI, 0.735-0.987; p = 0.03).

Conclusions. Ventricular diameters, end-systolic volume index and LVEF are related with improvements in myocardial contractility after dobutamine infusion, although only end-diastolic diameter was an independent predictor of contractile reserve. Thus, this parameter should receive particular attention in evaluations of the functional status of the myocardium in patients with NIDC.

Key words: *Cardiomyopathy. Echocardiograhy. Stress.*

Full English text available at: www.revespcardiol.org

Correspondence: Dr. M. Pérez-Paredes.
Unidad de Cardiología. Laboratorio de Ecocardiografía.
Hospital Universitario Morales Meseguer.
Avda. Marqués de los Vélez, s/n. 30008 Murcia. España.
E-mail: matiasperez@medynet.com

Received, 7 November 2002.
Accepted for publication, 3 July 2003.

Predictores de reserva contráctil miocárdica en pacientes con miocardiopatía dilatada no isquémica. Estudio mediante ecocardiografía de estrés con dobutamina

Introducción y objetivos. Los estudios de reserva contráctil con dobutamina han demostrado su utilidad en la valoración del estado funcional del miocardio. Sin embargo, no se conocen bien las variables asociadas a la presencia de reserva contráctil tras la estimulación inotrópica.

Pacientes y método. Con este fin, estudiamos a 50 pacientes (35 varones con una edad de 56,4 ± 9,5 años) con miocardiopatía dilatada no isquémica (MDNI), fracción de eyección (FE) de 28,7 ± 8,5% e índice de motilidad parietal (IMP) de 2,42 ± 0,34, a los que se realizó una ecocardiografía de estrés con dobutamina a dosis bajas. Se evaluó la respuesta contráctil mediante un parámetro diferencial obtenido de restar del índice de motilidad parietal basal el obtenido al pico del estrés (ΔIMP).

Resultados. Tras la dobutamina se obtuvo un IMP pico de 1,95 ± 0,58, pudiéndose calcular un ΔIMP medio de 0,45 ± 0,39. Ninguna variable clínica ni electrocardiográfica mostró relación con la presencia de reserva contráctil. Por el contrario, los diámetros telediastólico (p = 0,05) y telesistólico (p = 0,02), el índice de volumen telesistólico (p = 0,01) y la FE (p = 0,002) se asociaron con la presencia de reserva contráctil. En el análisis multivariable, únicamente el diámetro telediastólico se asoció de forma independiente con el grado de reserva contráctil (OR = 0,852; IC del 95%, 0,735-0,987; p = 0,03).

Conclusiones. Los diámetros ventriculares, el volumen telesistólico y la FE se relacionan con la mejoría de la contractilidad miocárdica tras la infusión de dobutamina, aunque únicamente el diámetro telediastólico es predictor independiente de la presencia de reserva contráctil. Por ello, este parámetro debe ser especialmente considerado a la hora de evaluar el estado funcional del miocardio en pacientes con MDNI.

Palabras clave: *Miocardiopatía. Ecocardiografía. Estrés.*

ABBREVIATIONS

DSE: dobutamine stress echocardiography.
LVEF: left ventricular ejection fraction.
WMSI: wall motion score index.
NIDC: nonischemic dilated cardiomyopathy.

INTRODUCTION

Dobutamine stress echocardiography (DSE) can be useful in evaluating myocardial function.[1-3] It has recently been shown that there is a relationship between the presence of contractile reserve assessed using DSE and medium-term survival in patients with nonischemic dilated cardiomyopathy (NIDC).[4] Patients with NIDC generally do not have a good prognosis, with high rates of morbidity and mortality in the short to medium term. The clinical management of these patients should therefore incorporate any tools which help to improve prognostic precision. The option of performing a family study should also be evaluated, as a substantial number of NIDC patients who go on to have a heart transplant have a family history of the disease.[5]

The aim of the present study was to analyze the relationship between clinical, electrocardiographic and echocardiographic (systolic and diastolic function) variables, and the presence of myocardial contractile reserve evaluated using DSE, in patients with NIDC.

PATIENTS AND METHODS

Patient selection

Nonischemic dilated cardiomyopathy was diagnosed according to World Health Organization guidelines[6] and patients were included prospectively in the study from in- or out-patient departments. Study inclusion criteria included: *a)* absence of previous heart disease and normal coronary arteries in the angiographic study (performed on inclusion in the study or within the previous two years); *b)* absence of valvular or congenital etiology; *c)* ejection fraction less than or equal to 40%, determined using echocardiography, and *d)* systolic dysfunction of at least four weeks' evolution. Exclusion criteria included having an inadequate acoustic window, an unstable clinical or hemodynamic profile, prior history of ventricular arrhythmias (sustained ventricular tachycardia or ventricular fibrillation), and patient's refusal to participate. The study protocol was approved by the center's Clinical Trials Committee. Informed consent to participate was requested from all patients. Sixty clinically stable patients with severe systolic dysfunction were studied initially, and 50 were finally included in the study. One patient was excluded due to inadequate acoustic window, three because they were clinically or hemodynamically unstable, and six patients refused to participate or were lost to follow-up.

Study design

Demographic, clinical and electrocardiographic data collected included age and sex, disease duration, functional status (assessed using the NYHA criteria), presence or absence of sinus rhythm and left bundle branch block, current medical treatment, and presence of co-morbid diabetes mellitus, arterial hypertension (AHT) and family history of cardiomyopathy. A baseline transthoracic echocardiogram was performed to measure systolic and diastolic function. This was followed by the low-dose dobutamine stress echocardiographic study.

Echocardiographic protocol

All studies were performed using a Sonos 5.500 (Philips) apparatus with harmonic imaging. Baseline echocardiographic variables included end-diastolic and end-systolic diameters, and ventricular volumes, measured with the area-length method and a 4-chamber view. The ejection fraction was calculated automatically from the volumes obtained by manual tracing of the left ventricular endocardial border in end-systole and end-diastole.[7] Diastolic function was measured by analyzing: *a)* mitral flow: E and A wave velocity, E/A ratio, E wave deceleration time and isovolumetric relaxation time; *b)* pulmonary venous flow: S, D and A' wave velocity, A' wave duration and S/D ratio, and *c)* color M-mode E-wave propagation velocity.

On completion of the baseline echocardiographic study, the four standard views were obtained in digital format using stress echocardiograph software, and dobutamine infusion was initiated using increasing doses (5, 10 and 20 μg/kg/min) administered in consecutive 5-minute phases. On completion of the stress protocol, off-line images were studied, and the peak wall motion score index (WMSI) was calculated. The WMSI was obtained by summing the score for each segment (1=normokinetic, 2=hypokinetic, 3=akinetic, and 4=dyskinetic) and dividing by 16, as recommen_ded in the American Society of Echocardiography guidelines.[7] Where left bundle branch block was present, scores were calculated by evaluating wall thickening but not wall motion. Dobutamine stress echocardiography was suspended before concluding the 20 μg dose if the drug was poorly tolerated, or where any of the following occurred: arterial hypertension (systolic arterial pressure >220 mm Hg and/or diastolic arterial

pressure >120 mm Hg), arterial hypotension (reduction of >30 mm Hg compared to baseline), supraventricular arrhythmias (supraventricular tachycardia or *de novo* atrial fibrillation, and ventricular arrhythmias (ventricular tachycardia or frequent polymorphic ventricular tachycardias). All studies were rated by 2 independent observers. In case of disagreement, segments were scored by consensus.

Contractile reserve in each segment was defined as an improvement in function of at least one point after inotropic stimulation. Global contractile reserve was assessed by subtracting baseline WMSI from peak WMSI after dobutamine infusion (ΔMSI). This parameter had a theoretic range of 0 (total absence of contractile response) to 3 (all dyskinetic segments become normokinetic). Contractile reserve was considered significant where ΔMSI≥0.44. This cut-point was recently validated by Pratali et al.[4]

Statistical analysis

Quantitative variables were expressed as means± standard deviations, and categorical variables were expressed as percentages. The Kolmogorov-Smirnov test with the Lilliefors correction was used to test whether quantitative variables were normally distributed. The χ^2 test was used to compare qualitative variables, and means were compared using Student's *t*-test. The relationship between systolic and diastolic function and the contractile reserve index was studied using Pearson's correlation coefficient. All comparisons were bivariate, and *P* values of <.05 were considered statistically significant. Variables with a value of *P*<.05 in the univariate analysis were included in a multivariate analysis using logistic regression. All analyses were performed using the SPSS 10.0 statistical package (SPSS inc. Chicago, USA).

RESULTS

Population

A total of 50 patients (35 men and 15 women) were included. Mean age was 56.4±9.5 years. On inclusion in the study, 10 patients (20%) were in NYHA functional class I, 34 (68%) were in class II and 6 (12%) were in class III. The electrocardiograph results showed that 39 patients (78%) had sinus rhythm, 8 (16%) had atrial fibrillation and 3 (6%) used pacemakers. A total of 29 patients (58%) had complete left bundle branch block. Three patients (6%) had type 2 diabetes, 17 (34%) had hypertension and 6 (12%) had a family history of dilated cardiomyopathy. Mean disease duration was 30.7±25 months (range, 1-120 months).

TABLE 1. **Baseline echocardiographic characteristics**

	Minimum	Maximum	Mean	Standard deviation
EDD, mm	45	72	59.2	6.6
ESD, mm	35	67	49.2	10.0
EDV, ml	122	404	167.2	67.7
ESV, ml	44	356	124.2	58.1
EF, %	11	40	28.7	8.5
E wave V, cm/s	11	121	58.3	23.2
A wave V, cm/s	5	139	67.5	24.9
E/A	1	2	0.75	0.5
E wave DT, ms	90	285	177.3	56.9
IVRT, ms	50	175	105.2	30.4
M-color Pv, cm/s	40	260	128.4	42.0
S wave V, cm/s	19	102	53.4	18.9
D wave V, cm/s	23	97	45.8	17.1
S/D	1	2	1.3	0.47
A' wave V, cm/s	20	195	34.2	28.2
A' wave T, ms	100	250	155.8	42.0
Baseline WMSI	1.6	3.0	2.42	0.34
Peak WMSI	1	2.8	1.95	0.58
ΔMSI	0.00	1.60	0.49	0.39

EDD indicates end-diastolic diameter; ESD, end-systolic diameter; EF, ejection fraction; WMSI, wall motion score index; CR, contractile reserve; T, time; DT, deceleration time; IVRT, isovolumetric relaxation time; V, velocity; PV, propagation velocity; EDV, end-diastolic volume; ESV, end-systolic volume.

General echocardiographic data

The group presented serious systolic dysfunction, with a mean ejection fraction (EF) of 28.7±8.5% and a baseline WMSI of 2.42±0.34. There were no relevant complications in terms of study procedures and all patients completed the study up to doses of 20 μg. Baseline echocardiographic values are shown in Table 1. After dobutamine infusion, mean peak WMSI was 1.95±0.58, and mean ΔMSI was 0.45±0.39. A total of 26 patients (52%) had preserved contractile reserve (ΔMSI>0.44), whereas 24 (48%) had not (ΔMSI<0.44).

Relationship between ΔWMSI and non-echocardiographic variables

None of the demographic variables or the clinical and electrocardiographic variables correlated with ΔMSI (Table 2). *P* values for correlations between age, sex and time with the disease and ΔMSI were 0.27, 0.37, and 0.60, respectively. NYHA functional class was likewise not associated with ΔMSI (*P*=.054), although a non-statistically significant tendency towards an improvement in function was observed in patients in class 1 after dobutamine infusion (ΔMSI of 0.73±0.56 for patients in class I vs 0.47±0.37 for the remaining patients).

TABLE 2. **Clinical and electrocardiographic variables and their relationship with ΔMSI**

	CR present (n=26)	CR absent (n=24)	*P*
Sex, M/F	20/6	15/9	.37
Sinus rhythm	20 (77%)	19 (79.1%)	.48
Atrial fibrillation	5 (19.2%)	3 (12.5%)	.47
LBBB	13 (50%)	16 (66.6%)	.25
Beta-blockers	17 (65.4%)	17 (70.8%)	.27
ACEI	25 (96.1%)	20 (83.3%)	.17
Diuretics	20 (77%)	21 (87.5%)	.25
Spironolactone	6 (23%)	11 (45.8%)	.06
Digoxin	8 (30.8%)	13 (54.1%)	.08
AIIRA	2 (7.7%)	3 (12.5%)	.33
Anticoagulants	7 (7.7%)	6 (25%)	1.00
Diabetes	1 (3.8%)	2 (8.3%)	.59
Hypertension	8 (30.7%)	9 (37.5%)	.56
Family history	2 (7.7%)	4 (16.6%)	.40

LBBB indicates left bundle branch block; ACEI, angiotensin converting enzyme (ACE) inhibitors; CR, contractile reserve.

Relationship between ΔMSI and monechocardiographic variables

In the univariate analysis, the end-diastolic (r=–0.46; *P*=.005) and end-systolic (r=–0.40; *P*=.002) diameters, the end-systolic volume (r=–0.43; *P*=.01) and the EF (r=0.44; *P*=.002) correlated significantly with the ΔMSI. None of the diastolic function parameters correlated with ΔMSI (Table 3). In the multivariate analysis, only end-diastolic diameter showed an independent association with the presence of contractile reserve (OR=0.852; 95% CI, 0.735-0.987; *P*=.03).

TABLE 3. **Relationship between ΔMSI and age, time with disease (in months) and baseline echocardiographic values**

	CR present (n=26)	CR absent (n=24)	*P*
Age, years	54.7	58.2	.27
Disease duration, months	27.9	32.1	.60
EDD, mm	56.8	62.0	.005
ESD, mm	45.2	53.7	.002
EDV, ml	153.0	183.0	.12
ESV, ml	104.6	146.4	.01
EF, %	31.7	24.3	.002
E wave velocity, cm/s	65.0	71.9	.30
A wave velocity, cm/s	74.1	60.5	.08
E/A	0.67	1.35	.051
E wave DT, ms	182.3	171.7	.55
IVRT, ms	106.9	103.3	.67
M-color Pv, cm/s	125.2	132.0	.58
S wave V, cm/s	52.2	54.8	.64
D wave V, cm/s	43.2	49.0	.25
S/D	1.28	1.33	.70
A' wave V, cm/s	36.8	31.0	.52
A' wave T, ms	143.4	170.3	.051
Baseline WMSI	2.30	2.54	.012
Peak WMSI	1.53	2.43	.000

EDD indicates end-diastolic diameter; ESD, end-systolic diameter; EF, ejection fraction; WMSI, wall motion score index; CR, contractile reserve; T, time; DT, deceleration time; IVRT, isovolumetric relaxation time; V, velocity; Pv, propagation velocity; EDV, end-diastolic volume; ESV, end-systolic volume.

Follow-up data

The primary endpoint was any of the following events: death, re-admission to hospital for cardiac insufficiency, worsening in functional class or need for a heart transplant. After a mean follow-up of 16.6±7.9 months, only 7 patients (14%) presented any of the events listed: one died (2%), one had worsening in NYHA functional class (2%) and 5 were admitted for heart failure (10%). None of the echocardiographic variables, including ΔMSI, were related to the primary endpoint. Of the clinical, ECG and demographic variables, only the presence of AHT was statistically significantly associated with a poorer evolution (33.3% incidence of events in patients with hypertension vs 6.4% in patients without hypertension; *P*=.029).

DISCUSSION

The aim of the present study was to identify clinical, electrocardiographic or echocardiographic parameters which predicted adequate functional response in the myocardium after inotropic stimulation with dobutamine. Dobutamine studies of myocardial contractile reserve have principally been performed in patients with ischemic cardiomyopathy, in an effort to show the presence of hibernating and therefore viable myocardium.[7] Similarly, DSE has been used to evaluate patients with systolic dysfunction before bypass surgery or percutaneous revascularization, and to establish a differential diagnosis between ischemic cardiomyopathy and NIDC.[8-10] Dobutamine stress echocardiography has also been used in patients with suspected tachycardiomyopathy stemming from atrial fibrillation to identify patients who recover function after cardioversion.[11]

In NIDC patients, the study of contractile reserve has been used in an attempt to predict late spontaneous recovery in patients with recent onset cardiomyopathy[2] or improvement in left ventricular systolic function after prolonged treatment with beta-blockers.[12] Comparisons with maximum O_2 consumption have also shown that DSE is useful in evaluating myocardial function in patients with advanced chronic heart failure.[13] In addition, increased survival has been observed in NIDC patients with an adequate myocardial response after dobutamine infusion.[4,14] However, few studies have attempted to explore the relationship between baseline clinical,

electrocardiographic or echocardiographic findings and the presence of contractile reserve.

Despite the prognostic importance of NYHA functional class in patients with NIDC,[15] in the present study no evidence of a statistically significant relationship between this parameter and the presence of contractile reserve was found. Nevertheless, a non-significant tendency towards an improvement in function was observed after dobutamine infusion in patients in class I: with a greater number of patients this variable may have achieved statistical significance. The DSE showed no relationship between age, sex, time with the disease, presence of sinus rhythm or left bundle branch block, medical treatment used, or the presence of associated factors such as diabetes or arterial hypertension and myocardial contractile response. On the other hand, the echocardiographic parameters were related with contractile response. Our findings indicate that smaller ventricular (end-diastolic and end-systolic) diameters and smaller baseline end-systolic volumes lead to a greater capacity for contractile response in stimulated myocardium. Baseline EF was also related with this response: patients with a more depressed EF showed a weak inotropic response after dobutamine infusion. Of all the echocardiographic variables included in the multivariate analysis, only end-diastolic diameter correlated independently with the presence of contractile reserve. This finding highlights the importance of this parameter when evaluating myocardial function when serious systolic dysfunction is present.

Previous studies have shown that a restrictive diastolic pattern and a reduction in E wave deceleration time are associated with poorer evolution and higher mortality in patients with congestive heart failure.[16-18] In our series, there was no association between any of the diastolic parameters and inotropic response measured with the ΔMSI. This may be at least partially explained by the fact that all of the patients included were clinically and hemodynamically stable on entry in the study (88% were in NYHA functional class I or II), were receiving optimal medical treatment, and that most showed altered diastolic relaxation patterns with A wave>E and a relatively long E wave deceleration time (177.33±56.9 ms).

The possible effect of treatment with beta-blockers on the results of this test deserves special mention, as the expression of the beta-adrenergic receptors is altered in patients with congestive heart failure, with a tendency for beta-1 receptors to be internalized and beta-3 receptor density to increase. It has been suggested that the recovery of beta-1 receptors and the blocking of beta-3 receptors (and consequent negative inotropic effect) may at least partially explain the beneficial effects of treatment with beta-blockers.[19,20] The modulating effect of beta-blockers on the expression and stimulation of those receptors suggests that these drugs influence the results of tests such as the DSE, which are based on adrenergic stimulation. In the present study, however, the proportion of patients taking beta-blockers was similar in the group which responded to dobutamine (n=17; 65.4%) and in the group which did not (n=17; 70.8%), indicating that there was no association between the presence of the drug and the test results (*P*=.27).

Finally, the fact that there was no relationship between presence of contractile reserve and prognosis during follow-up is probably due to the small number of patients in the study, as well as to their clinical and hemodynamic stability and the low rate of recorded events. Interestingly, having a prior history of AHT was associated with a worse prognosis, despite optimal treatment.

Study limitations included the fact that the evaluation of segmental contractility in echocardiography is influenced by observer subjectivity. To mitigate this, all of the studies were performed by the same echocardiographer (MPP) and interpreted by three observers (MPP, AC, DMG). Differences of opinion were resolved by consensus. On the other hand, the fact that a significant number of patients did not have a sinus rhythm or had complete left bundle branch block further complicated interpretation of the studies. This limitation was ameliorated as far as possible by seeking inter-observer agreement when interpreting the echocardiograms, and by excluding non-interpretable cases. Likewise, greater importance was given to myocardial thickening than to systolic excursion when each segment was scored, particularly when there was evidence of paradoxical wall movement.

CONCLUSIONS

Baseline ventricular diameters, end-systolic volume and left ventricular ejection fraction correlated significantly with improvements in myocardial contractility after dobutamine infusion, although only end-diastolic diameter independently predicted the presence of contractile reserve. This parameter is of particular relevance when myocardial function is evaluated in patients with nonischemic dilated cardiomyopathy. Future studies should investigate whether periodic monitoring of this parameter would be useful in determining prognosis in these patients.

REFERENCES

1. Pierard LA, Hoffer EP. Role of stress echocardiography in heart failure. Am J Cardiol 1998;81:G111-4.
2. Kitaoka H, Takata J, Yabe T, Hitomi N, Furuno T, Doi YL. Low dose dobutamine stress echocardiography predicts the improvement of left ventricular systolic function in dilated cardiomyopathy. Heart 1999;81:523-7.
3. Scrutinio D, Napoli V, Passantino A, Ricci A, Lagioia R, Rizzon P. Low-dose dobutamine responsiveness in idiopathic dilated cardiomyopathy: relation to exercise capacity and clinical outcome. Eur Heart J 2000;21:927-34.
4. Pratali L, Picano E, Otasevic P, Vigna C, Palinkas A, Cortigiani L, et al. Prognostic significance of the dobutamine echocardiography test in idiopathic dilated cardiomyopathy. Am J Cardiol 2001;88:1374-8.
5. Monserrat L, Hermida M, Bouzas B, Mosquera I, Mahon N, Peteiro J, et al. Miocardiopatía dilatada familiar en pacientes trasplantados por miocardiopatía dilatada idiopática. Rev Esp Cardiol 2002;55:725-32.
6. The WHO/ISFC task force on the definition and classification of cardiomyopathies. Br Heart J 1980;44:672-3.
7. Schiller NB, Shah PM, Crawford M. Recommendations for quantification of the left ventricle by two-dimensional echocardiography. American Society of Echocardiography Committee on Standars, Subcommittee on Quantification of Two-Dimensional Echocardiograms. J Am Soc Echocardiogr 1989;2:358-67.
8. Senior R, Kaul S, Lahiri A. Myocardial viability on echocardiography predicts long-term survival after revascularization in patients with ischemic congestive heart failure. J Am Coll Cardiol 1999;33:1848-54.
9. Rimbaldi R, Hamburger JN, Geleijnse ML, Poldermans D, Kimman GJ, Aiazian AA, et al. Early recovery of wall motion abnormalities after recanalization of chronic totally occluded coronary arteries: a dobutamine echocardiographic, prospective, single-center experience. Am Heart J 1998;136:831-6.
10. Cohen A, Chauvel C, Benhalima B, Guyton P, Desert I, Valty J. Is dobutamina stress eschocardiography useful for non-invasive differentiation of ischemic from idiopatic dilated cardiomyopathy? Angiology 1997;48:783-93.
11. Paelinck B, Vermeersch P, Stockman D, Convens C, Vaerenberg M. Usefulness of low-dose dobutamine stress echocardiography in predicting recovery of poor left ventricular function in atrial fibrillation dilated cardiomyopathy. Am J Cardiol 1999;83:1668-71.
12. Ramahi FM, Longo MD, Cadariu AR, Rohls K, Carolan AS, Engle KM, et al. Left ventricular inotropic reserve predicts improvement in ejection fraction after long-term carvedilol therapy in non-ischemic cardiomyopathy [abstract]. Circulation 1999;100: I203.
13. Paraskevaidis IA, Tsiapras DP, Adamopoulos S, Kremastinos DT. Assesment of the functional status of heart failure in non ischemic dilated cardiomyopathy: an echo-dobutamine study. Cardiovasc Res 1999;43:58-66.
14. Pratali L, Otasevic P, Bojic D, Cortigiani L, Palinkas A, Csanady M, et al. Prognostic significance of dobutamine echo test in idiopathic dilated cardiomiopathy [abstract]. Circulation 1999;100: I644.
15. Madsen BK, Videbaek R, Stokholm H, Mortensen LS, Hansen JF. Prognostic value of echocardiography in 190 patients with chronic congestive heart failure. A comparison with New York Heart Association functional classes and radionuclideventriculography. Cardiology 1996;87:250-6.
16. Parameshwar J, Keegan J, Sparrow J, Sutton GC, Poole-Wilson PA. Predictors of prognosis in severe chronic heart failure. Am Heart J 1992;123:421-6.
17. Xie GY, Berk MR, Smith MD, Gurley JC, De Maria AN. Prognostic value of Doppler transmitral flow patterns in patients with congestive heart failure. J Am Coll Cardiol 1994;24:132-9.
18. Xie GY, Berk MR, Smith MD, De Maria AN. Relation of Doppler transmitral flow patterns to functional status in congestive heart failure. Am Heart J 1996;131:766-71.
19. Gauthier C, Tavenir G, Charpentier F. Functional beta-3 adrenergic receptor in human heart. J Clin Invest 1996;98:556-62.
20. Khan NUA, Movahed A. Papel de los betabloqueadores en la insuficiencia cardíaca congestiva. CHF 2000;6:299-312.