Prognostic Evaluation in Patients with Systolic Dysfunction: Functional and Echocardiographic Evaluation

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Introduction and objectives. Multiple clinical and echocardiographic parameters have been shown to have prognostic value in cases of left ventricular dysfunction. The purpose of this paper was to evaluate the relative predictive power of such parameters.

Methods. Ninety-one patients with systolic dysfunction were prospectively studied. Functional status was evaluated using the New York Heart Association classification and the 6-minute walking test. Other clinical and biochemical parameters were assessed, and an anatomic and functional echocardiographic study was performed.

Results. Mean follow-up was 16.5 months (SD: 6.95). Eighteen patients died and two underwent heart transplantation (cardiac death 22%). Multiple regression analysis showed that the only independent predictor of death was functional status. Functional classes I and II showed a 16-month mortality rate of 10%, class III 40% and class IV 83%. The mortality rate was 67% for patients who walked < 300 meters and 0% for those who reached > 500 meters. When echocardiographic results were analyzed separately, the only independent predictors of outcome were left atrial diameter and the E wave deceleration time. Deceleration times < 100 ms or atrial diameters > 5 cm were associated with a mortality rate of 46%. The correlation between E wave deceleration time and the walking test was r = 0.55, p < 0.0001.

Conclusions. Functional status is the main predictor of outcome in patients with systolic dysfunction, whether assessed subjectively or estimated objectively by a walking test. Among echo-Doppler parameters, the deceleration time of the E wave and left atrial diameter gave similar prognostic information, although with less statistical significance. They can confirm or substitute the prognosis obtained by the functional classification.

Key words: *Echocardiography. Prognosis. Heart failure.*

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Valoración pronóstica de los pacientes con disfunción sistólica: estudio funcional y ecocardiográfico

Introducción y objetivos. Es conocido el valor pronóstico de múltiples parámetros clínicos y ecocardiográficos para la disfunción ventricular. Nuestro propósito fue estudiar esos parámetros para valorar su potencia predictiva relativa.

Métodos. Estudiamos prospectivamente 91 casos de disfunción sistólica. Se valoró la situación funcional: clase funcional de la NYHA y la prueba de marcha de 6 min. Se analizaron criterios clínicos, analíticos, así como anatomofuncionales mediante ecocardiografía.

Resultados. El seguimiento fue de 16,5 meses (DE: 6,95). De causa cardíaca murieron 18 pacientes y dos recibieron trasplante (muerte cardíaca: 22%). El análisis de regresión múltiple demostró como único predictor independiente de mortalidad la situación funcional. La clase funcional presentó una mortalidad a los 16 meses para las clases I-II, III y IV del 10, 40 y 83%. La prueba de la marcha presentó una mortalidad del 67% para quienes caminaron < 300 m, y del 0% en los que recorrieron > 500 m. Analizando sólo el ecocardiograma, los únicos predictores independientes fueron el tiempo de desaceleración de la E y el diámetro auricular izquierdo. Tiempos de desaceleración < 100 ms, o diámetros auriculares > 5 cm indicaron una mortalidad del 46%. La correlación entre el tiempo de desaceleración de E y la duración de la marcha presentó un valor de r = 0,55, y de p < 0,0001.

Conclusiones. La situación funcional es el dato pronóstico clave en la disfunción sistólica, ya de forma subjetiva, ya objetiva mediante la prueba de la marcha. El tiempo de desaceleración de la E y el tamaño auricular aportan una información pronóstica similar, aunque con menos significación estadística. Puede confirmar o sustituir la valorada según la clasificación funcional.

Palabras clave: *Ecocardiografía. Pronóstico. Insuficiencia cardíaca.*

INTRODUCTION

Ventricular dilation associated with systolic dysfunction is the common endpoint of most diseases of the heart. Generally speaking, its appearance

denotes a poor prognosis for the patient, with a high risk of death in the years after diagnosis. That risk continues to be high in spite of the remarkable advances that have taken place in the treatment of this syndrome.[1] Patients with systolic dysfunction and ventricular dilation are a mixed group that includes pathological conditions due to many different causes and patients in very different clinical situations.[2-4] This means that, although the prognosis of the group is generally poor, there are notable differences in the evolution of each patient that should be recognized in clinical practice, both when deciding on therapeutic measures and informing patients. Various prognostic predictors have been described, including functional class,[5] etiology,[4,5] neurohormonal factors,[6] natremia,[7] ventricular[8] and left atrial dimensions,[9] ejection fraction,[10,11] parameters of diastolic function,[11-17] right ventricular measurements[17-19] and, more recently, the 6-min walking test[20,21] and end-systolic parietal stress.[22] This information is applicable to all or some of these patients, and can have different pathophysiological meanings. The multiplicity of predictors can cause confusion at the time of evaluating patients.

Functional clinical assessment and the identification of markers of diastolic function by echocardiography are parameters that are easy to determine and should provide a fast and simple way to evaluate the prognosis of patients with systolic dysfunction. Parting from this hypothesis, the aim of this study was to assess the usefulness of these parameters, which were selected out of a large group of clinical and echocardiographic parameters, as predictors of the evolution of patients with left ventricular systolic dysfunction, and to understand and compare their interrelations.

MATERIAL AND METHODS

Study population

Consecutive patients seen in the echocardiography laboratory of a tertiary hospital, diagnosed as systolic dysfunction with ventricular dilation in the study requested, were included for follow-up. This diagnosis was made when the left ventricular (LV) end-diastolic diameter was greater than 5.6 cm and the ejection fraction (EF) was less than 50%, and was the only inclusion criterion for follow-up. Data were collected from June to November 1996. The sample included 93 patients with a mean age of 63.5 years (standard deviation [SD], 8.8; range, 37 to 78), 39% hospitalized and 61% outpatients.

Follow-up

All the patients who were included in the study remained under the care of their regular doctors, with the treatment prescribed by them, except that angiotensin-converting enzyme inhibitors (ACEI) were used whenever they were tolerated. With the previous consent of patients, telephone contact was maintained with them every three months in order to interrogate them about the follow-up variables: functional class, hospital admissions, and survival. When the study was finalized, the clinical history of each patient included was reviewed to verify the admission data, functional evaluation of the physicians, and cause of death, as needed. In the deaths that occurred outside the hospital, details on the death were obtained from family members and the death certificate. Two patients who died of non-cardiac causes, with no relation to the disease (one glioblastoma and one case of multiple injuries), were excluded from the study so all relative values were referred to a final group of 91 cases.

Follow-up parameters

Parameters of functional status

The functional class was determined in the interrogation and classified according to the criteria of the New York Heart Association (NYHA).[23] The walking test was made by instructing the patient to walk a route of known length for 6 min, the result being the total distance covered in that time.[20,21]

Clinical and analytical parameters

The etiology was labeled as ischemic when there was evidence of ischemic heart disease in the clinical manifestations or exercise stress test, areas of evident infarction in the echo, or severe lesions in the catheterization; otherwise, the case was classified as

non-ischemic. Heart rate and blood pressure were determined at the time that the echocardiogram was made, after 5 min of rest in left lateral supine position. The rest of the clinical information was obtained by means of the interview, so only previously diagnosed diabetics were considered. Creatinine, sodium, and potassium were determined in blood samples obtained at the time of onset of the follow-up. A posteroanterior chest radiograph was made in standing position and forced inspiration. The finding of venocapillary hypertension or interstitial infiltrate was evaluated by two cardiologists using criteria of vascular redistribution and/or interstitial infiltrate. When discrepancies were found, the disagreement was resolved by consensus. Both physicians were unaware of the rest of the patient´s data. An ECG strip was recorded in lead II to determine the rhythm of the patient. The treatment of patients in the 3 months preceding the event or study closure was recorded.

Echocardiographic parameters

All echocardiographic studies were made by the same operator, who did not know the clinical condition of the patient. The studies of the hospitalized patients were carried out after their situation had stabilized. The echocardiographic study was made in left lateral supine position with an ATL ultramark 9 echograph (Advanced Technologies Laboratories Inc., U.S.) and a 3.5-MHz probe. The left cavities were measured by guiding the M-mode sector from a longitudinal parasternal section, according to the recommendations of the North American Society of Echocardiography.[24] Ventricular mass was determined using the Devereux formula.[25] From the 4-chamber apical plane the short axis of the right ventricle (RV) was measured in end-systole and end-diastole, just above the tricuspid valve. The RV shortening fraction was obtained as the ratio of the difference between the previous measurements and the end-diastolic length of the short axis. In the same plane, the area of regurgitant flow through the tricuspid valve was measured as the combined area of turbulence and laminar flow. The degree of mitral insufficiency was determined by means of the proximal convergence method, as is described in detail in another article.[26] Ventricular filling was recorded as the minimum pulsed Doppler sample volume between points of the mitral valve.[27] Isovolumetric relaxation time (IRT) was measured in a pulsed Doppler recording made in a 4-chamber and aorta plane, placing the sample volume on the ventricular face of the septal leaflet of the mitral valve, and enlarging it to include simultaneous recording of the filling and

ejection flows; IRT was measured from the end of the ejection flow to the beginning of the E wave.[28] To estimate the systolic pressure of the pulmonary artery, continuous Doppler was used to record the maximum speed of the regurgitant flow through the tricuspid valve in an apical plane. To the right ventriculoatrial gradient obtained was added 10 mm Hg to obtain the pulmonary artery pressure.[29] The curve of the flow velocity of mitral insufficiency was recorded in a 4-chamber plane with continuous Doppler to obtain dP/dt. The curve should have a clear profile to the point of maximum velocity. Maximum dP/dt was estimated using the Bargiggia method,[30] and minimum dP/dt with a method developed by our group.[31] Cardiac output was evaluated with the combined method, using the measurement of the area of the LV outflow tract obtained from its radius measured in the longitudinal parasternal plane and the integral of ejection flow recorded with pulsed Doppler in the same place, the 4-chamber and aorta plane.[32] End-systolic parietal stress was calculated from LV measurements in M-mode and blood pressure, using the Reicheck formula.[33] The slope of E-wave deceleration was defined as the ratio between maximum E-wave velocity and the duration of deceleration, measured from the peak of the wave to the ideal point of intersection with the 0 velocity line.

STATISTICAL ANALYSIS

The statistical analysis was carried out with the SPSS 8.0® and PRESTA packages. The follow-up endpoints considered were the presence or absence of two variables: *a)* cardiac death, including death of cardiac origin and heart transplantation (from here on, when we refer to mortality, we will be talking about cardiac death), and *b)* cardiac event during follow-up, including death, heart transplantation, and admission for heart failure. In the groups in which one of the endpoints was reached, the continuous variables were compared using the Student t test for independent variables. The difference between groups was determined using variance analysis (one-way ANOVA) and the Bonferroni test for quantitative values and contingency tables, applying the χ^2 test for dichotomic values. In order to evaluate the mean duration of event-free survival, Kaplan-Meier analysis was used. To analyze the relation between diverse variables and survival, univariate analysis of the Cox regression was used. The Cox regression with multiple variables was used with the conditional anterograde method to determine the independent variables. The variables that could only be measured in certain situations were not included. For example, systolic

TABLE 1. **Comparison of mean values of continuous variables in patients with and without cardiac death**

	N	Cardiac death	Alive	P
Walking test, m	85	310.8 (109.7)	421.0 (64.5)	.000
EF, %	91	28 (8.3)	33.2 (8.7)	.054
LA, cm	91	5.3 (0.6)	4.7 (0.7)	.000
Creatinine, mg/dl	91	1.43 (0.46)	1.18 (0.32)	.030
RVEDD, cm	91	4.06 (0.77)	3.73 (0.64)	.049
RVESD, cm	91	3.04 (0.88)	2.68 (0.72)	.059
EV, cm/s	91	97.5 (28.5)	76.5 (20.9)	.000
AV, cm/s	61	50.2 (26.7)	70.2 (27.7)	.023
EV/AV	61	2.4 (1.2)	1.3 (0.9)	.001
E dec., cm/s^2	91	8.3 (3.1)	5.5 (2.9)	.000
EDT, ms	91	121.2 (38.0)	149.8 (45.0)	.010
IVRT, ms	91	94.1 (24.5)	120.2 (25.7)	.000
PSP, mm Hg	65	54.7 (7.7)	46.5 (8.4)	.036

The values between parentheses indicate standard deviation. LA indicates left atrium; EF, LV ejection fraction; RVEDD, right ventricular end-diastolic diameter; RVESD, right ventricular end-systolic diameter; EV, maximum E-wave velocity; AV, peak A-wave velocity; EV/AV, EV to AV ratio; E dec., slope of E-wave deceleration; EDT, E-wave deceleration time; IVRT, isovolumetric relaxation time; PSP, pulmonary artery systolic pressure. The values of the variables not shown present non-significant differences.

pulmonic pressure was not used because it requires the existence of tricuspid insufficiency and its inclusion would lead to population selection. This condition affected the systolic pressure values of the pulmonary artery, dP/dt measurements, and A wave of the E/A ratio. The selection of some of the cutoff points that appear in the results was made with ROC curves, as will be described. A value of *P*<.05 in a two-tailed study was considered statistically significant, except for the Bonferroni test, in which a significance of *P*<.02 was required.

RESULTS

The patients in the sample had a mean age of 63.5 years (SD, 8.8; range, 37-78 years). The group was composed of 85.7% men, 23.6% diabetics, 18.9% smokers, and 11.2% regular drinkers. The cause was considered ischemic in 49.5% of the patients. The EF was 32.0% (SD, 8,6%). Forty-one percent (41%) presented findings of heart failure. ACEI treatment was given to 84%, diuretics to 77%, spironolactone to 6%, and beta-blockers to 35%. At the beginning of follow-up, 66% of patients were in NYHA functional classes I or II, with 67% of them with sinus rhythm, 25.2% atrial fibrillation, and 7.8% with a permanent pacemaker.

The mean follow-up time of the patients was 16.5 months (SD, 6.95; median, 18 months; range, 1-29 months), during which 18 patients (19.8%) died of cardiac causes, 2 suddenly (2.2%) and 16 from heart failure (17.6%). Two patients underwent heart transplantation (2.2%). Considering sudden death to be death produced by congestive heart failure and heart transplantation, a cardiac mortality of 22% was observed. Seventeen patients suffered a single episode of heart failure that required hospital admission (18.7%) and 14 had more than one episode (15.4%). Considering all admissions, transplantations, and deaths, 58 patients (63.7%) were event-free.

A comparison of the mean values of the continuous variables between the patients who remain alive and those who suffered cardiac death is shown in Table 1. Only the variables with the most significant differences are shown. The most statistically significant differences were found in the results of the walking test, all the parameters of diastolic function, and the left atrial dimensions, all of which had *P* values close to .001. There were also differences in the plasma creatinine values, RV end-diastolic diameter, and systolic pulmonic pressure. The EF was smaller in patients with cardiac death, although this was non-significant. The results were very similar when the same parameters were compared between the groups with and without events. The analysis of categorical variables disclosed no differences in coronary risk factors (smoking habit, diabetes, sex) between patients

TABLE 2. **Analysis of the differences in discrete variables between the groups of patients with and without cardiac mortality**

	Cardiac death (%)	Alive (%)	P
Functional class III versus III-IV	10.0 versus 48.4	90.0 versus 51.6	.000
No CHF episode versus one or more CHF episodes	3.3 versus 61.3	96.7 versus 38.7	.000
TI not III versus III-IV	16.4 versus 50.0	83.6 versus 50.0	.005
MI not III versus III-IV	15.9 versus 40.7	84.1 versus 59.3	.011
No Rx infiltrate versus Rx infiltrate	13.6 versus 75.0	86.4 versus 25.0	.001

CHF indicates congestive heart failure; TI, tricuspid insufficiency; MI, mitral insufficiency; Rx, chest radiograph.
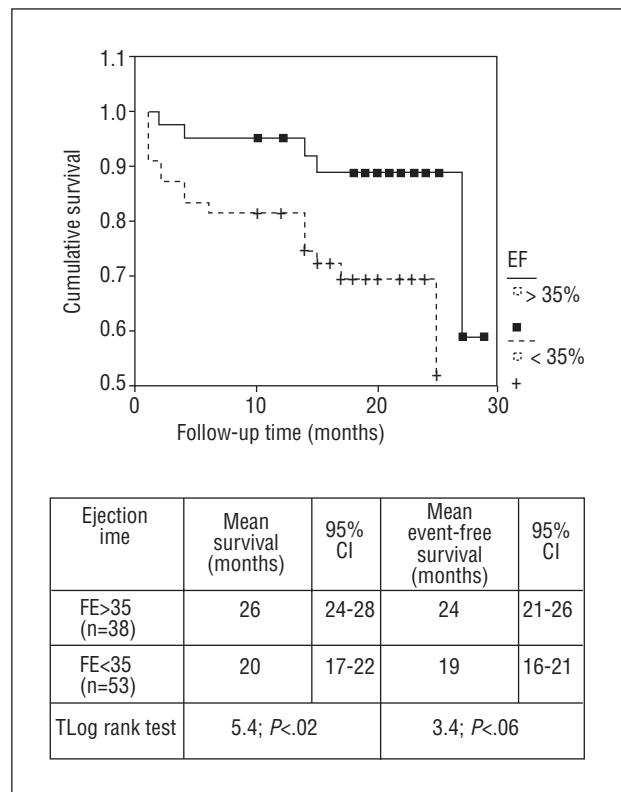
TABLE 3. **Prognostic significance of each variable for cardiac mortality by Cox regression (univariate analysis)**

Variable	Hazard ratio (95% CI)	P
Functional class III-IV	9.46 (3.13-28.60)	.0000
Distance walked*	1.02 (1.01-1.02)	.0000
Distancia less than 300 m	17.9 (4.98-64.4)	.0000
Admissions for CHF	348.65 (2.50-48714)	.0000
Congestion in chest radiograph	23.78 (0.01-109453)	.12
Heart rate	1.02 (0.99-1.05)	.16
Creatinine	3.95 (1.16-13.45)	.04
Sodium*	1.16 (1.01-1.34)	.05
Left atrium	3.96 (2.15-7.30)	.0000
LV diastolic diameter	2.19 (1.18-4.06)	.02
LV ejection fraction	1.00 (0.96-1.04)	.99
RV diastolic diameter	2.08 (1.06-4.07)	.03
RV systolic diameter	1.86 (1.04-3.31)	.04
RV shortening fraction*	1.03 (0.98-1.08)	.20
End-systolic parietal stress	1.01 (0.99-1.02)	.17
Mitral insufficiency III-IV	4.03 (1.61-10.10)	.003
Tricuspid insufficiency III-IV	4.61 (1.86-11.39)	.002
E-wave velocity	1.04 (1.02-1.06)	.0000
E-wave deceleration time*	1.02 (1.01-1.03)	.0001
E-wave deceleration slope	1.30 (1.14-1.49)	.0001
Isovolumetric relaxation time*	1.04 (1.02-1.06)	.0000
Pulmonic systolic pressure	1.08 (1.00-1.16)	.04

*The sign of the variable was changed to obtain risks greater than 1. RV indicates right ventricle; LV, left ventricle: CHF, congestive heart failure.

Ejection ime	Mean survival (months)	95% CI	Mean event-free survival (months)	95% CI
FE>35 (n=38)	26	24-28	24	21-26
FE<35 (n=53)	20	17-22	19	16-21
TLog rank test	5.4; P<.02		3.4; P<.06	

Fig. 1. Kaplan-Meier survival curves for cardiac mortality in relation to ejection fraction (EF). The adjacent table shows how the mean survival of patients with EF>35 was greater than that of patients with a poorer EF. The difference was not significant for event-free survival.
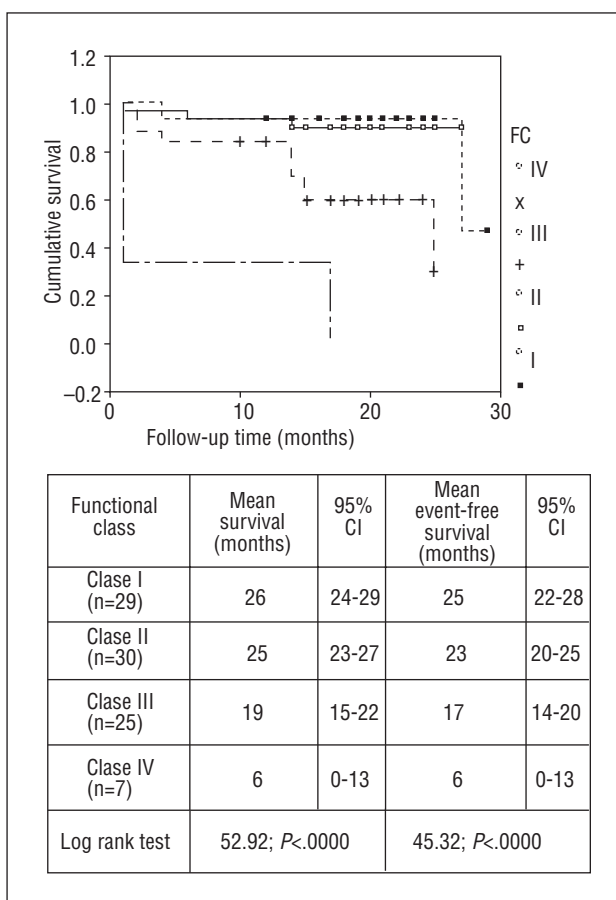
with cardiac mortality and survivors. The only significant difference in treatment is that high-dose diuretic treatment was more frequent in the group of patients who died (29% versus 8%; P=.05). There were differences in the functional class, history of heart failure, presence of a radiographic infiltrate, and degree of mitral and tricuspid insufficiency (Table 2). When the presence or absence of events was considered, the differences were similar, except for etiology. Events were more frequent during the follow-up in patients with ischemic heart disease (56% versus 28%; P<.03).

Univariate Cox regression analysis was performed to assess the influence of a number of variables on survival. The most significant results are shown in Table 3. The results were practically the same when cardiac death or total events were considered as endpoints. None of the epidemiological parameters achieved statistical significance when included in the regression equation (age, sex, smoking habit, alcohol use, etiology, diabetes).
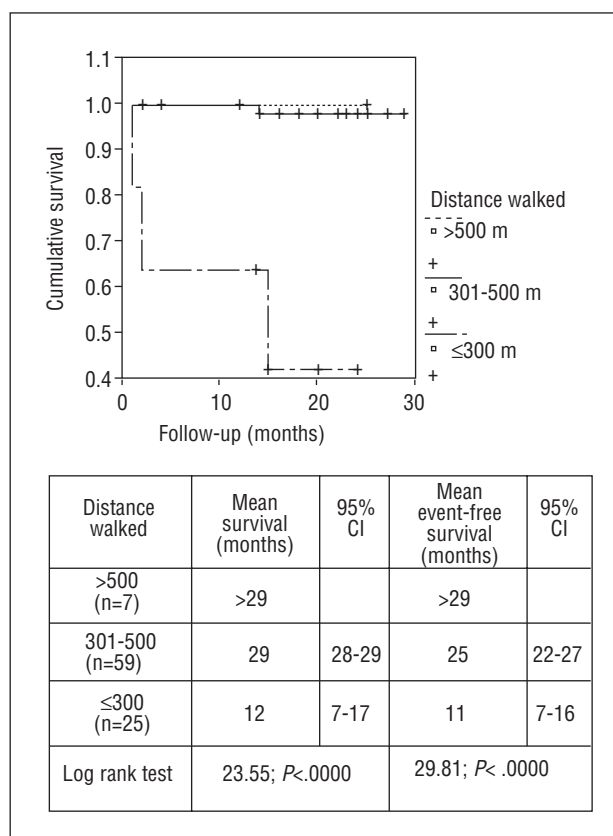
In Figures 1 to 5 are shown the Kaplan-Meier survival curves for the variables with the most significant clinical and statistical results. The figures also show the survival table for cardiac death and events. Survival in a mean follow-up period of 16 months was lower in patients with EF<35% (20 months versus 26 months; Figure 1). This cutoff point was selected using ROC curves. It also was smaller in patients with functional classes IV and III (9 and 16 months versus 25 and 26 months for classes II and I; Figure 2) and in patients who walked less than 300 m in the walking test (12 versus 29 or more months; Figure 3). The cutoff point of 300 m was selected based on findings in the literature[15], and the 500-m cutoff point was chosen for its 100% specificity for the absence of events. Likewise, patients with deceleration times of less than 100 m lived less time (17 versus 26 or more months; Figure 4). In this case, the cutoff points were assessed with ROC curves and were adjusted to the hundredths. The evolution was worse in patients with atrial diameters of more than 5 cm (20

Functional class	Mean survival (months)	95% CI	Mean event-free survival (months)	95% CI
Clase I (n=29)	26	24-29	25	22-28
Clase II (n=30)	25	23-27	23	20-25
Clase III (n=25)	19	15-22	17	14-20
Clase IV (n=7)	6	0-13	6	0-13
Log rank test	52.92; P<.0000		45.32; P<.0000	

Fig. 2. Kaplan-Meier survival curves for cardiac mortality according to functional class (FC). The adjacent shows how survival and event-free survival are worse in functional class III and IV, with respect to classes I and II.

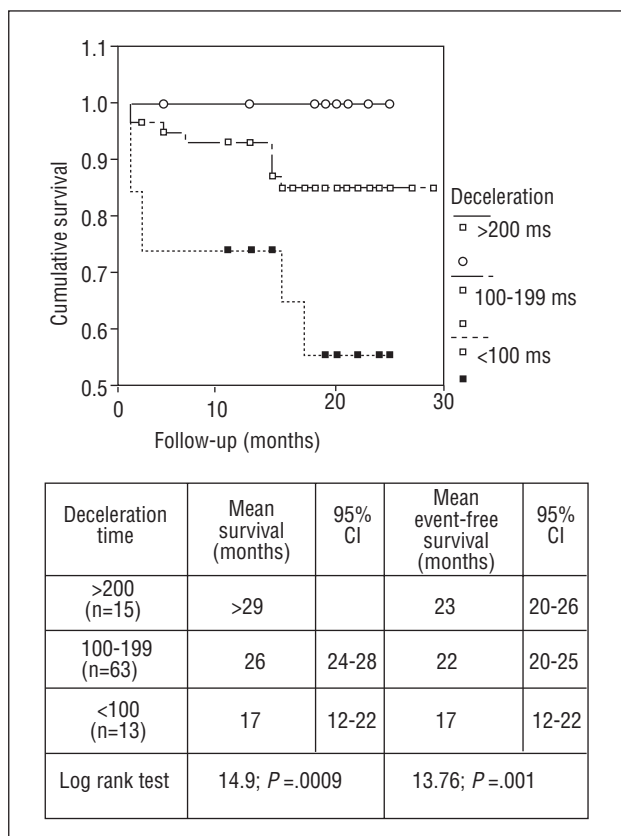| Distance walked	Mean survival (months)	95% CI	Mean event-free survival (months)	95% CI
>500 (n=7)	>29		>29	
301-500 (n=59)	29	28-29	25	22-27
≤300 (n=25)	12	7-17	11	7-16
Log rank test	23.55; P<.0000		29.81; P< .0000	

Fig. 3. Kaplan-Meier survival curves for cardiac mortality in relation to distance walked. The following table shows how survival and event-free survival get worse as the distance that patients are capable of walking decreases.
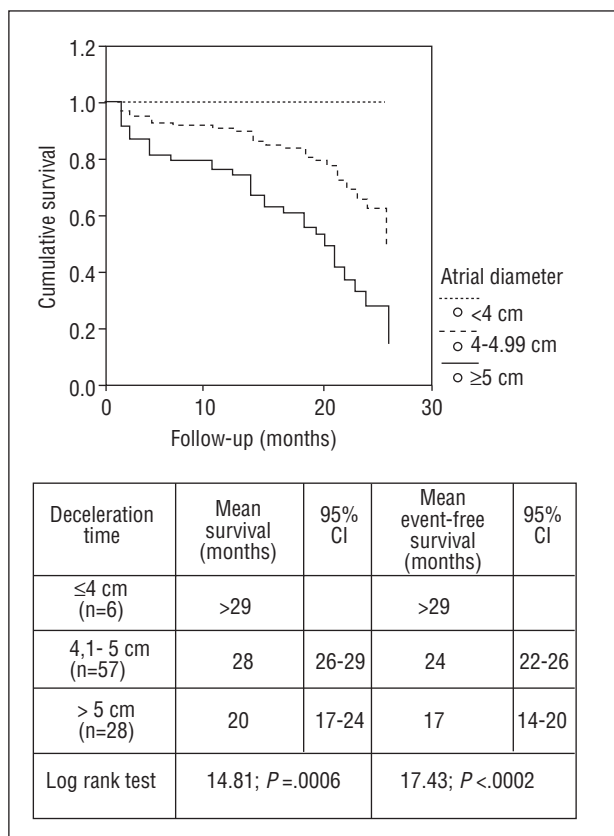
versus 28 months or more; Figure 5). The cutoff points were selected according to the normal value of the atrium in the longitudinal parasternal plane (4 cm) and the 5-cm value was chosen because of its 100% specificity for the absence of events.

The mortality during follow-up was greater in patients with an EF of less than 35% (30% versus 13%; $P=.057$), worse functional class (83%, 46%, 10%, and 10% for classes IV, III, II, and I, respectively; $P<.000$; the difference was not significant when comparing functional classes I and II), less distance walked (67%, 19%, and 0% for those that walked less than 300 m, 300 to 500 m, and more than 500 m, respectively; $P<.001$; the differences between the last two groups were not significant), shorter deceleration times (46%, 19%, and 7% for times of less than 100 m, 100 to 200 m, and more than 200 m, respectively; $P<.01$; the differences between the last two groups were not significant), and greater left atrial diameters (46%, 14%, and 0% for atria of more than 5 cm, 5 to 4 cm, and less than 4

cm, respectively; $P=.003$; the differences between the last two groups were not significant).

A significant correlation was found between the deceleration time of the E wave and the distance walked in the walking test ($r=.55$; $P<.0001$).

The multivariate analysis to determine the parameters that were related most closely to cardiac mortality demonstrated that functional class excluded the rest ($P<.0001$) from the equation (Table 4). Nevertheless, considering that those who could not do the walking test due to a functional limitation walked less than 300 m, this test became more powerful than the clinical assessment of functional class, with a hazard ratio of 17.92 (95% confidence interval [CI], 4.98-64.49). If the patients in functional class IV were excluded, since 6 of the 7 patients in functional class IV did not perform the walking test, it continued to be the most powerful. Patients incapable of walking 300 m had a hazard ratio of 4.1 (95% CI, 2.2-7.7). When only echocardiographic measures were included in the analysis, the only ones that entered the regression

Deceleration time	Mean survival (months)	95% CI	Mean event-free survival (months)	95% CI
>200 (n=15)	>29		23	20-26
100-199 (n=63)	26	24-28	22	20-25
<100 (n=13)	17	12-22	17	12-22
Log rank test	14.9; P =.0009		13.76; P =.001	

Fig. 4. Kaplan-Meier survival curves for cardiac mortality in relation to deceleration time. The adjacent table shows how survival and event-free survival worsen as the E-wave deceleration time decreases.

Deceleration time	Mean survival (months)	95% CI	Mean event-free survival (months)	95% CI
≤4 cm (n=6)	>29		>29	
4,1- 5 cm (n=57)	28	26-29	24	22-26
> 5 cm (n=28)	20	17-24	17	14-20
Log rank test	14.81; P =.0006		17.43; P <.0002	

Fig. 5. Kaplan-Meier survival curves for cardiac mortality in relation to left atrial diameter. The following table shows how survival and event-free survival worsen as the size of the atrium increases.

equation were the E-wave deceleration time (hazard ratio 1.199; 95% CI, 1.0293-1.3988) and left atrial dimensions (hazard ratio 3.9491; 95% CI, 1.6674-9.3530). The rest of the echocardiographic variables were excluded from the study.

DISCUSSION

In our study, functional class was the only independent predictor of cardiac mortality, although it was replaced by the distance covered in the walking test in view of the fact that patients incapable of carrying out the test walked less than 300 m. The echocardiographic parameters, although of great prognostic value, did not provide information in addition to that obtained with the functional class or walking test. When only the echocardiographic parameters were assessed, the only independent predictors were E-wave deceleration time and left atrial dimensions, the rest of the echocardiographic variables being excluded.

Contributions of the study

In the last 10 years, studies have been published on the prognostic value of various clinical and echocardiographic parameters in LV systolic dysfunction. The interest of our work lay in determining the predictors of prognosis in a simpler, more powerful, and independent way. This can help to organize diagnostic protocols for the selection of parameters, as well as to determine which protocols can replace others that cannot be obtained, in spite of their interest.

Functional class is and has been the fundamental reference criterion for classifying patients with systolic dysfunction and deciding on their therapy, especially with regard to performing heart transplantation in class IV patients.[34,35] The fact that functional class was the only independent predictor in our group undeniably supports this. It was capable of discriminating three well-defined prognostic groups, so that the mortality at 16 months was 10% in patients of functional classes I and II, 40% in class III, and

83% in class IV. In that sense, a clear discrimination between patients in classes II and III was found that other studies have not demonstrated.[36] The functional class is evaluated through the interview, which adds a load of subjectivity. The walking test is a way to objectively assess functional capacity. Although it has been demonstrated that, in absence of analysis of oxygen consumption, it is less related with the evolution of patients, it also has been observed that the fit between oxygen consumption and distance walked correlated with accuracy in patients with a depressed functional capacity.[20] Its advantage with respect to the oxygen consumption test lies in its simplicity, since it does not require any instruments. It is noteworthy that an objective test was less useful than a subjective one. An explanation could be that only 1 in 6 patients in class IV could carry out the test. When class IV was excluded from the analysis, the walking test was a more powerful predictor of event-free survival than functional class. For patients in class IV, the impossibility to carry out the test would be a finding of poor prognosis. If we consider of 300 m as a limit, a shorter walking test separates the populations with mean survivals of 11 months (95% CI, 7-16) and 25 months (95% CI, 23-27), with a relative risk of 4.1 (95% CI, 2.2-7.7).

Our study emphasizes the prognostic importance of clinical data that are easily obtained, such as a history of admission for heart failure or the radiological findings of pulmonary congestion, and recalled the value of others, such as plasma creatinine and the hyponatremia, that have been described previously.[7] A clinical finding of interest was the fact that a different prognosis was observed in patients with atrial fibrillation. The only study that analyzed patients in atrial fibrillation found no differences in their prognosis.[10] The fact that the risk factors considered did not show an influence on the evolution of patients may indicate that in advanced stages of myocardial damage, the condition itself, rather than its causes, is what determines the evolution.

LV systolic dysfunction had an adverse prognosis, and the patients in our sample showed a cardiac mortality of 22% at 16 months. Nevertheless, in the study of patients with systolic dysfunction, other parameters aside from the degree of dysfunction were more relevant prognostic indicators. In fact, in our sample, the degree of systolic dysfunction, as measured by the EF, had less predictive value than the parameters of diastolic function or functional status, and were excluded by these parameters in multivariate studies. Two of the echocardiographic parameters introduced in this study had not been analyzed

previously as predictors of evolution, the maximum and minimum value of dP/dt, which can only be obtained in patients with mitral insufficiency. The maximum value of dP/dt reflects systolic function, and has a different dependency on load than the parameters of ejection phase,[37] such as EF or cardiac output. The dP/dt is less dependent on postload than EF and cardiac output, so in a situation like dilated cardiomyopathy, in which postload is elevated, it could add interesting information.[38] The possible prognostic value of dP/dt was not confirmed in our study.

The parameters of diastolic dysfunction were closely related with survival, principally left atrial pressure, which masks many data related with ventricular relaxation.[39,40] It is not very likely that the parameters that reflect relaxation are useful for predicting prognosis. The minimum value of dP/dt is closely linked to ventricular relaxation,[31] and was not shown to be useful in discriminating the prognosis of patients. In our experience, the speed of propagation of the E wave measured with color M was unrelated to the prognosis of patients with systolic dysfunction,[41] although this parameter was not included in this study. The prognostic value of other, more recent, parameters is not known, such as tissue Doppler of the mitral annulus.[42] In contrast, all the parameters of diastolic function that indicate an increase in atrial pressure, including left atrial dilation, were associated closely with the evolution of patients and their functional capacity. We demonstrated the good correlation between the walking test and time of deceleration. Deceleration times of less than 100 m or atrial diameters of more than 5 cm indicate a mortality of 46% at 16 months, whereas the mortality of patients who had both criteria reached 54%. Most studies have obtained similar findings with respect to the importance of parameters of diastolic function.[10-16] Since all of them showed similar pathophysiological phenomena, we think that some of these measurements can be dispensed with in this type of studies, especially the most variable ones, like isovolumetric relaxation time or E/A ratio, which cannot be measured in patients in atrial fibrillation and do not contribute more information than measures made exclusively on the E wave.

As in other studies, we found prognostic value in the degree of mitral and tricuspid insufficiency, the systolic pressure of the pulmonary artery, and RV systolic function. The main determinant of systolic pulmonic pressure in patients with systolic dysfunction is left atrial pressure,[43] so there again appears to be a pathophysiological connection

between the elevation of atrial pressure and other disorders of prognostic value, such as pulmonic hypertension and RV dilation. In our study, RV dilation and dysfunction did not appear as independent predictors, in contract with other studies.[17-19] Nevertheless, it is undeniable that the RV muscle can be affected primarily, which is why it seems feasible that RV function would be an independent predictor, depending on the group or size of the population selected.

Comparison with other studies

It is difficult to establish comparisons between different samples, including studies of the survival of patients with systolic dysfunction. Some studies include patients in atrial fibrillation,[10,12] at the same time that they only include idiopathic cardiomyopathy. Others only consider patients with a given functional status[18] or only with severely depressed EF.[10,13] To this must be added the difficulty of comparing the results of multivariate analysis in which the variables included and method of inclusion are different. In spite of the difficulties of comparing results from the literature, there is coherence between studies. The mortality of the patients in our sample was 19.8% in a mean follow-up of 16 months, which is less than, but not very different from, the mortality observed in studies that included patients in atrial fibrillation (21% to 27% at 2 years[10,12]), patients with sinus rhythm and without ischemia (19%, in the study of De Groote et al[18]), or consecutive patients with EF less than 40% (14% at one year in the study of Xie et al[13]). This supports the idea that once ventricular dysfunction develops the condition itself determines prognosis, not its cause. This allows patients with different etiologies and risk factors to be combined in the same sample, as we have done. With regard to predictors of evolution, the parameters of diastolic function and atrial size appear to be fundamental markers of prognosis in almost all the studies we have found, except that of Rihal et al.[10] EF is a predictor in only a few studies, whereas other parameters, like end-systolic parietal stress[22] or right ventricular measurements,[17-19] have not been studied much.

Limitations

The inclusion of heart transplantation as cardiac death could be discussed. As in other studies, it was decided that it should be considered a terminal cardiac situation that requires cardiac death to save the life of the patient. Be that as it may, the small number of

TABLE 4. **Multivariate analysis of the categorical variable functional class (FC), using functional class I as reference**

	Hazard ratio	**95% CI**
FC II	2.78	0.25-30.63
FC III	22.93	2.81-187.17
FC IV	81.27	9.20-717.85

heart transplantations in our study (2 patients) means that their impact on the final result is negligible.

Our study was made in a tertiary hospital, a reference hospital for more complex pathologies. This could mean that our sample had different characteristics from other populations, and possibly a higher mortality. The comparison with other published studies did not disclose large differences, although it should be taken into account.

The variability of ventricular filling parameters with different load conditions and even ventilation was considered a limitation.[44,45] Nevertheless, it has been demonstrated that this variability is mild in patients with chronic heart failure when the measurements are made without abrupt manipulation of the load.[46] The changes produced by abrupt manipulation have also demonstrated their prognostic usefulness,[47,48] although they could not be assessed in this study because they were not included in the protocol.

Measurements of RV systolic pressure and dP/dt could only be obtained in patients with mitral and tricuspid insufficiency, and were more easily obtained in cases of greater insufficiency. The presence of atrioventricular valve insufficiency in itself entails a worse prognosis, so the inclusion of the measurement makes it difficult to assess patients with a better prognosis. Something similar occurs with the walking test in patients with functional class IV. In our study, measurements of pulmonic pressure or dP/dt were excluded from the multivariate analysis. A second analysis was made for the walking test, in which a test result of less than 300 m was interpreted as indicating that patients were incapable of walking due to their functional class.

CONCLUSION

The clinical evaluation of the patient was found to be fundamental in the prognostic assessment, and functional class provided key information. The walking test, atrial measurements, and E-wave deceleration time can confirm the prognosis obtained from the functional evaluation, or replace it when it is

unclear.

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