

Predicting Heart Failure and Mortality in Chronic Chagas' Heart Disease. A Novel Disorder in Spain

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Over the last 20-30 years more than a million people have emigrated from Latin America to Spain.¹ Among these was a certain number who contracted Chagas disease in their country of origin - some of whom later developed heart problems. In Europe, Chagasic cardiomyopathy is an exotic disease, and can present difficulties in its clinical management. This has been highlighted recently in the *Revista Española de Cardiología*, in which a consensus document of the Sociedad Española de Medicina Tropical y Salud Internacional regarding the management of patients with Chagas disease was published.² Nearly all studies involving large numbers of Chagas seropositive subjects (Ch+) agree that about three quarters remain asymptomatic and enjoy a favorable long-term clinical outcome, while the remaining 25% develop symptoms with an associated high mortality.

The diagnostic triad suggestive of Chagas disease includes: a) epidemiological history; b) positive serology in at least 2 tests; and c) clinical findings such as heart failure, syncope, complex arrhythmias, embolisms, electrocardiographic findings such as right bundle block, left anterior hemiblock, a combination of the latter 2 conditions, ventricular extrasystoles, ST-T segment anomalies, and apical aneurysm of the left ventricle, among others.

The traditional New York Heart Association (NYHA) functional classification (I-IV) can be used to reflect an improvement or worsening in patient clinical status. However, a recent consensus document³ has added 4 irreversible stages of heart damage (A-D, similar to that used to describe the status of patients with cancer) to this

system. This staging may be applied to the work of Petti et al published in the current issue of the *Revista Española de Cardiología*, as shown below.

Systolic Dysfunction

In the present study by Petti et al,⁵ which involved an initial 2990 Ch+ patients, 95 (3.18%) asymptomatic subjects were selected on the basis of showing echocardiographic signs of left ventricular dysfunction (structural damage without heart failure; NYHA I, stage B) in order to determine the risk factors that predict progression to heart failure (NYHA II-IV stages C or D, structural damage with prior/current/ heart failure, or heart failure resistant to treatment). The mean follow up time was 5 years. Among 13 clinical, electrocardiographic, and echocardiographic variables analyzed by Cox multivariate analysis, only severe systolic dysfunction and the mitral E-septum separation were found to be statistically significant (both of which are easy to estimate in the rural setting). Left ventricular dysfunction was grouped semi-quantitatively as mild, moderate, or severe, rather than quantitatively (ejection fraction). Mortality was 3% (3/95) among those patients who remained asymptomatic, but was 37% (10/27) among those who developed heart failure.

The final analysis did not include 2033 Ch+ asymptomatic subjects (68%) who were in the so called "indeterminate" stage of the disease with no evidence of heart failure (NYHA I; stage A), nor 762 patients (25.5%) in NYHA functional class II-IV, stages C or D.

The present work differs from previous multivariate analyses of patients with Chagas disease in that it tries to predict the development of heart failure; the others only analyzed predictors of mortality. The papers published in this area,⁶⁻¹⁴ which include a total of 3507 patients including the present work, all confirm that the degree of systolic dysfunction (ejection fraction) is a highly significant predictor of mortality, even though these studies differed in the risk factors analyzed, the number of patients involved, the severity of ventricular systolic deterioration shown, and the inclusion of both asymptomatic patients and those with advanced heart

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disease. Variables such as clinical group or NYHA functional class^{8,10,12,13} male sex,¹² age at admission,¹³ and maximum oxygen consumption have all been recorded as significant.⁷ Among the electrocardiographic variables examined, non-sustained ventricular tachycardia during 24 h Holter monitoring,^{12,13} low QRS voltage¹², and a prolonged QT segment⁹ have been reported significant, while among the echocardiographic variables the end systolic and diastolic dimensions of the left ventricle,^{9,13} cardiomegaly,¹² the shortening fraction, and the mitral-septal separation have been reported as important.⁸

Two recent papers^{12,13} have used independent prognostic factors obtained by Cox analysis with the aim of estimating mortality using a scoring system. In a study involving 424 subjects in which 139 deaths were recorded over a mean follow-up time of eight years, Rassi et al¹² identified 6 significant variables: NYHA functional class III or IV (5 points), cardiomegaly (5 points), echocardiographic left ventricular systolic dysfunction (3 points), non-sustained ventricular tachycardia during 24 h Holter monitoring (3 points), a low voltage QRS segment (2 points), and male sex (2 points). Patients were then assigned to one of 3 risk groups: low risk (0-6 points), intermediate risk (7-11 points), and high risk (12-20 points). Mortality at 10 years was 10%, 44%, and 84% respectively. It should be pointed out that this work included a "validation series" from another hospital. In another study involving 856 patients that excluded those presenting with heart failure, Viotti et al¹³ recorded 18 deaths after a follow-up period of 8 years. These authors propose a clinical score system reflecting the risk of progress of chronic Chagasic myocarditis that takes into account the following: left ventricular systolic diameter >40 mm or systolic dysfunction (3 points), sustained ventricular tachycardia (3 points), age at admission >50 years (2 points), intraventricular conduction abnormalities (2 points), and benzonidazol treatment (-2 points). Patients with a score of 10 points are at maximum risk while those with 0 are at no risk. The prognostic significance of secondary or primary right ventricular dysfunction remains to be determined.¹⁴

Diastolic Dysfunction

Diastolic dysfunction is normally estimated by pulsed Doppler analysis of the mitral valve and pulmonary veins, and by studying the myocardial shortening, and lengthening velocities by tissue Doppler (TD) analysis of the mitral ring. In one study, a group of 126 patients with chronic Chagasic cardiomyopathy showed a strong correlation between the deterioration of diastolic function and the left ventricular ejection fraction with increasing left ventricular and left atrial size.¹⁵ Patients with a pseudonormal filling pattern have larger left ventricular dimensions, decreased myocardial contractility, and a smaller left ventricular ejection fraction. Tissue Doppler analysis distinguishes patients with normal ventricular

filling from those with a pseudonormal pattern and high left ventricular diastolic pressures.¹⁶ In patients with Chagas disease showing a normal ECG and normal 2 dimensional echocardiographic results, TD has also detected the prolongation of left and right ventricular contraction and isovolumetric relaxation as signs of early myocardial involvement. In fact, a normal ECG does not exclude early myocardial involvement.⁴ However, the prognostic value of these findings is unknown.

Conclusions

Systolic dysfunction of the left ventricle and other echocardiographic variables are of great value in predicting the development of heart failure in asymptomatic patients with Chagas disease, as has been shown in other work.

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