Left Ventricular Global Performance and Diastolic Function in Indeterminate and Cardiac Forms of Chagas' Disease

Antônio Pazin-Filho, PhD, Minna M. Dias Romano, MD, Rogério Gomes Furtado, MD, Oswaldo César de Almeida Filho, PhD, André Schmidt, PhD, José Antonio Marin-Neto, PhD, FACC, and Benedito Carlos Maciel, MD, PhD, FACC,
São Paulo, Brazil

The majority of patients with Chagas' disease remain for 10 to 30 years in the indeterminate form (IF) of this disease. They have no symptoms, serologic positivity, normal electrocardiogram results and heart size, and normal left ventricular global and segmental systolic function on 2-dimensional echocardiography. To investigate whether this group of patients have any impairment of left ventricular global performance (Tei index) and diastolic function, we have studied 43 individuals (age 49 ± 12 years) including 14 healthy volunteers and 29 patients with Chagas' disease divided as IF (n = 12) and cardiac form (n = 17). Echocardiographic measurements included ejection fraction, Tei index, left atrial volume index, transmitral (peak early transmitral flow velocity, late peak mitral velocity, tissue Doppler, late peak mitral velocity duration) and pulmonary (systolic pulmonary vein velocity, diastolic pulmonary vein velocity, retrograde pulmonary vein velocity, retrograde pulmonary vein velocity duration) flow velocities, and tissue Doppler velocities at lateral mitral annulus (peak early transmitral flow velocity, late peak mitral velocity, systolic pulmonary vein velocity). Although ejection fraction and S′ velocity were significantly lower for patients with cardiac form compared with control and IF groups, Tei index was not able to differentiate patients with cardiac conditions from the other groups. Diastolic dysfunction was documented for patients with cardiac form by left atrial volume index, early transmitral peak velocity, early expansion wave by tissue Doppler, late expansion wave by tissue Doppler, and peak early transmitral flow velocity/early expansion wave by tissue Doppler. Patients with the IF of Chagas' disease did not show any abnormality of diastolic function. Thus, when the IF is further characterized on the basis of absence of any echocardiographic marker of regional systolic dysfunction, no impairment of diastolic function can be detected. (J Am Soc Echocardiogr 2007;20:1338-1343.)

Chagas' disease remains a significant public health issue in several countries and is a major cause of morbidity and mortality in Latin America.[1] Chagas' disease consists of acute and chronic phases. In the chronic phase most patients show the so-called indeterminate form (IF) of the disease, which usually lasts 10 to 30 years. After this period approximately 30% to 40% of the patients develop overt cardiac disease.[2] Although chagasic megaesophagus and megacolon produce typical clinical conditions in roughly 5% to 10% of patients, Chagas' cardiomyopathy is by far the most serious form of the disease. Progression of myocardial dysfunction in the chronic phase of the disease is heterogeneous, usually unpredictable, and tends to be slow.[2] However, when cardiac involvement is manifest, there is strong evidence that the mortality associated with Chagas' disease is clearly related to the severity of myocardial dysfunction.[3]

Why many patients remain throughout life with the IF whereas others progress into chronic complications constitutes one of most intriguing features of Chagas' heart disease.[4] Thus, the traditional concept of the IF of Chagas' disease requires only that asymptomatic patients showing positive serology tests have normal physical examination and electrocardiogram (ECG) results and normal heart, esophagus, and colon radiograph findings.[5,6] However, in almost all studies addressing the IF of Chagas' disease the inadequate characterization of the indeterminate phase is certainly responsible for discrepant results reporting on cardiac involvement in this group of patients and showing some degree of cardiac abnormality in a substantial number of these patients.

We have previously shown that patients classified in the IF of Chagas' disease according to its classic definition, but showing minor left ventricular (LV) regional dysynergy on echocardiogram, have a defi-

From the Division of Cardiology, Department of Internal Medicine, University Hospital, Medical School of Ribeirão Preto, University of São Paulo, São Paulo, Brazil.

Reprint requests: Benedito Carlos Maciel, MD, PhD, FACC, Division of Cardiology, Department of Internal Medicine, Medical School of Ribeirão Preto, 14048-900 – Ribeirão Preto – SP – Brazil (E-mail: *bcmaciel@fmrp.usp.br*).

0894-7317/$32.00

doi:10.1016/j.echo.2007.04.029

nite impairment of LV contractility, as evaluated by the slope of the LV end-systolic pressure-dimension relationship.[7] Moreover, we also showed that, independent of the clinical classification, patients who had minor LV segmental wall-motion abnormalities on baseline 2-dimensional (2D) echocardiogram presented a more depressed myocardial contractility when compared with patients who had only isolated conduction abnormalities on the ECG.[7] Furthermore, we have demonstrated that minor LV wall-motion abnormalities documented at baseline 2D echocardiography in patients with Chagas' disease who have normal global systolic function are a definite predictor of deterioration of ventricular function during follow-up.[8]

Although diastolic dysfunction has been previously reported in patients with Chagas' disease,[9-14] in these studies patients were classified based only on the presence or absence of ECG abnormalities and considering only the pattern of mitral flow velocities. LV global and segmental systolic function as evaluated by 2D echocardiography has not been used to classify patients with various clinical forms of Chagas' disease in those investigations. In the current study, we evaluated the presence of diastolic dysfunction in patients with IF and cardiac form (CF), as compared with a group of control subjects, using a more rigid clinical definition of the IF; patients with specific positive serology tests should have no symptoms, normal ECG findings and heart size on chest radiographs, and normal global and segmental LV systolic function on 2D echocardiography.[15] In particular, we also investigated the ability of the Tei index[16] to detect LV global performance abnormality in this setting.

METHODS

Study Group

In all, 43 participants were evaluated in this study, including 14 healthy volunteers who composed the control group (13 male, 92.8%; 41.6 ± 8.5 years) and 29 patients with Chagas' disease divided into the following groups. IF group was composed of 12 patients (10 male, 83.8%; 47.8 ± 10.4 years) who had no cardiac or digestive symptoms, and showed normal ECG findings, normal esophagus and chest radiography results, and normal Doppler 2D echocardiographic study findings. The CF group was composed of 17 patients. This group was further divided into a group (group CF-1; 7 patients; 1 male; 54.4 ± 16.3 years) presenting diffuse myocardial systolic dysfunction on echocardiographic examination and a second group (group CF-2; 10 patients; 6 male; 51.1 ± 10.7 years) with preserved global systolic ventricular function but showing segmental systolic dysfunction on 2D echocardiography isolated (n = 6) or associated to ECG abnormalities (n = 4). No patient with Chagas' disease had current or previous clinical manifestations of heart failure. The protocol was approved by the institutional ethics committee. All those who were included in this investigation provided written informed consent. None had diabetes, hypertension, or any other kind of cardiovascular involvement.

Study Protocol

M-mode and 2D echocardiograms and Doppler analysis were performed in all participants using a commercially available ultrasound system (Sonos 5500, Philips, Andover, Mass) with a S4 (2-4 MHz) transducer. Two-dimensional images were obtained in parasternal long- and short-axis views and in apical 4- and 2-chamber views. M-mode measurements of aorta, left atrium (LA), right ventricle, and LV diastolic and systolic dimensions, in addition to diastolic dimension of the interventricular septum and the LV posterior wall, were obtained in all participants. Global systolic LV function was evaluated by quantifying ejection fraction using Simpson's method on apical 2- and 4-chamber views. Segmental wall-motion analysis was performed classifying each of 16 LV segments (anterior, lateral, posterior, and septal segments in 3 levels: basal, mid, and apical) as presenting normokinesia, hypokinesia, akinesia, or dyskinesia. Diastolic function indexes based on Doppler velocities and tissue Doppler (TD) velocities were obtained according to published recommendations.[17] Doppler echocardiographic variables included: LA volume index, transmitral (peak early transmitral flow velocity [E], late peak transmitral flow velocity [A], TD, A duration) and pulmonary vein (systolic pulmonary vein velocity, diastolic pulmonary vein velocity, retrograde pulmonary vein velocity [Ar], Ar duration) flow velocities, and TD velocities at lateral mitral annulus (early expansion wave by tissue Doppler [E′], late expansion wave by tissue Doppler [A′], maximum systolic expansion wave by tissue Doppler [S′]). The Tei index was calculated as the sum of the isovolumic contraction time and isovolumic relaxation time divided by ejection time as previously described.[16] Each measurement was evaluated in triplicate and the mean values of each variable were used in the statistical analysis.

Data Analysis

We initially compared the systolic and diastolic ventricular function variables among the 4 groups and, later, we performed the same evaluation among the 3 groups with preserved systolic LV function. Although age was not significantly different among the groups in the first two analyses, because of its strong influence over diastolic function, especially TD parameters, we performed the analysis again for the group of participants with preserved systolic ventricular function, considering only patients with age into the range of 30 to 59 years.

Statistical Analysis

All data are presented as mean ± SD. Nonparametric Kruskal-Wallis test with Dunn's multiple comparisons test, when applicable, was used to compare continuous variables, whereas qui-square test was used to compare