Ventricular tachycardia during exercise testing as a predictor of sudden death in patients with chronic chagasic cardiomyopathy and ventricular arrhythmias

Angelo A V de Paola, J Anthony Gomes, Armenio B Terzian, Mauro H Miyamoto, Eulogio E Martinez Fo

Abstract
Objective—To verify the prognostic value of exercise induced ventricular arrhythmias in patients with chagasic cardiomyopathy.

Methods—69 consecutive patients (37 male, 32 female; age range 21–67 years) with chronic chagasic cardiomyopathy and ventricular arrhythmias (more than 10 ventricular premature complexes per hour) were evaluated during treadmill exercise testing, using the Bruce protocol. Protocol end points were peak heart rate or presence of sustained ventricular tachycardia.

Main outcome measure—Sudden cardiac death.

Results—44 patients (group I) developed ventricular tachycardia during exercise testing (five sustained and 39 non-sustained), and 25 did not (group II). After a follow up of 24 (SD 15) months sudden cardiac death occurred in seven patients in group I and in none in group II (P < 0·05).

Conclusions—Ventricular tachycardia on exercise testing is significantly associated with sudden cardiac death in patients with chronic chagasic cardiomyopathy and ventricular arrhythmias.

Keywords: chagasic cardiomyopathy, ventricular tachycardia, exercise testing

Exercise results in a series of alterations which can increase circulating catecholamines and the sympathetic drive to the heart.1 These physiological changes can affect the myocardium and initiate a ventricular arrhythmia, specially in patients with cardiac disease and left ventricular dysfunction.2 However, the clinical value of exercise testing for patients with ventricular arrhythmias and coronary heart disease is not established.

Chagas disease is one of the most important cardiac diseases in South America.3 Left ventricular dysfunction, ventricular arrhythmias, and autonomic changes are common findings in this disease4 and sudden death is an important problem in areas where the disease is endemic.5

The prognostic importance of ventricular arrhythmias during exercise testing has been studied in patients with coronary artery disease.6–10 The significance of exercise induced arrhythmias has not been reported in Chagas disease. This study was undertaken to verify the prognostic value of exercise induced ventricular arrhythmias in patients with chagasic cardiomyopathy.

Methods
DEFINITIONS
Chronic chagasic myocarditis was defined as the presence of chronic cardiomyopathy and a positive Machado Guerreiro serum complement and haemaglutinin test.

Ventricular tachycardia was defined as ≥ 3 sequential ventricular complexes at a rate of >100/min. If this arrhythmia lasted more than 30 seconds or resulted in cardiovascular collapse, it was defined as sustained ventricular tachycardia; if not it was considered to be non-sustained ventricular tachycardia.

PATIENTS, MATERIALS, AND PROCEDURES
The study population included 69 patients with chronic chagasic cardiomyopathy and ventricular arrhythmias. All patients had their antiarrhythmic drugs discontinued for at least five half lives and had more than 10 ventricular premature beats per hour or at least one episode of ventricular tachycardia during a 24 hour Holter monitoring. Three of these patients were on amiodarone therapy (low dose of 200 mg orally per day) and the drug was discontinued for one month before the patient entered the protocol. There were no patients receiving β blocker therapy. There were 37 men and 32 women, with ages ranging from 21 to 67 years (mean 46, SD 12, years). Thirty two patients had palpitations, 16 had syncope, and seven had clinical documentation of sustained ventricular tachycardia or ventricular fibrillation. Forty eight patients had a history of congestive heart failure; of these 39 were in New York Heart Association (NYHA) class II, and nine were in class III or IV. Each patient was in a compensated state before entering the protocol.

Echocardiography was performed in all patients and ejection fraction was calculated by the Pombo method.11 Patients suspected of having coronary artery disease underwent a coronary angiography study. No patient had any other identifiable organic heart disease.

Treadmill exercise testing—Exercite testing was performed on a motor driven treadmill...
Relation between testing. СuVT, No clinical palpitation syncope VT during EF < VT CHF class block Bifascicular Palpitations CHF, congestive CHF class Syncope 16 < 100 VPC/Holter 294 05 (8%) CHF class > II 48 05 (8%) CHF class = I 21 04 (19%) Syncope 16 02 (12%) No syncope 53 05 (9%) Palpitations 32 04 (12%) No palpitation 37 05 (8%) Clinical SuVT 07 02 (28%) No clinical SuVT 62 05 (8%) Bifascicular block 34 05 (14%) No bifascicular block 35 02 (5%) >100 VPC/H on Holter 43 04 (9%) <100 VPC/H on Holter 26 03 (11%) EP < 0-40 22 02 (9%) EP > 0-40 47 05 (10%) VT during ET 44 07 (16%) P < 0-05 No VT during ET 25 00

CHF, congestive heart failure; VPC, ventricular premature complexes; EF, left ventricular ejection fraction; SuVT, Sustained ventricular tachycardia; VT, ventricular tachycardia; ET, exercise testing.

Arrhythmias during exercise testing Two patients did not have any arrhythmia during exercise; 10 (14%) had isolated premature ventricular beats, 13 (18%) had couples, 39 (56%) had non-sustained ventricular tachycardia, and five (7%) had non-sustained and sustained ventricular tachycardia. The four patients with complete AV block were pacemaker dependent during exercise; all of them developed arrhythmias during exercise testing: one couplets, two non-sustained ventricular tachycardia, and one sustained ventricular tachycardia. There was no change in the QTc interval during exercise when compared with control values.

Medical therapy and clinical outcome Patients were seen in an arrhythmia research clinic by one of the investigators every three months. Mean follow up was 24 (15) months. Thirty six patients (52%) were off drugs. Antiarrhythmic drugs were prescribed to patients with clinical sustained ventricular arrhythmias, syncope, and inducible ventricular arrhythmias and for those with disabling palpitations. After completing clinical and laboratory evaluation 33 patients (48%) were on antiarrhythmic drugs because of symptoms: 23 patients on amiodarone, three on quinidine, three on propafenone, one on amiodarone and propafenone, one on dysopiramid, and two on phenytoin. During a mean follow up of 24 months 12 patients died; seven of these had sudden cardiac death. Of the patients with sudden death, five were on drug therapy (three on amiodarone, one on propafenone, and one on dysopiramid).

Ventricular tachycardia during exercise testing was the only variable that significantly influenced sudden cardiac death in this study population (table). Discussion Regardless of the mechanisms of cardiac arrhythmias the sympathetic nervous system and circulating catecholamines are very important in arrhythmogenesis. The adrenergic state can suppress or provoke cardiac arrhythmias; serious arrhythmias can be provoked or exacerbated by exercise. Also, patients with exercise induced ventricular tachycardia may be more sensitive to plasma noradrenaline than other patients. The majority of these reports are from patients with coronary heart disease; in some there is a correlation between the occurrence of exercise induced ventricular arrhythmias and significant coronary artery disease and impairment of left ventricular function. On the other hand patients with exercise induced non-sustained ventricular tachycardia and normal cardiac function have a good prognosis. However, the clinical significance of exercise testing in patients with ventricular arrhythmias remains poorly defined.

Chronic chagasic myocarditis is a cardiac
neuromyopathy with sympathetic ganglion
denervation and dysfunction of the parasympathetic autonomic control of the heart.16
This gradual autonomic denervation in chronic Chagas cardiomyopathy can partially
explain sudden death in some patients.17

Our study population was ambulatory and
two thirds of them had a left ventricular ejection
fraction above 40% and only 13% had class III or IV congestive heart failure. These
patients with only mild left ventricular dys-
function were different from the usual referral
cases, where sustained ventricular tachycardia,
 disabling symptoms, and severe left ventricular dysfunction were more common.5

Additionally, the autonomic dysfunction and
the sympathetic reserve of the heart was prob-
bly better than in more advanced cases of
Chagas cardiomyopathy. Whether the degree of autonomic dysfunction and catecholamine sensitivity explains the results of our study
remains unclear. Nonetheless, ventricular
tachycardia during exercise testing was the
only variable which was significantly associ-
ated with sudden cardiac death in our study
population with chronic chagasic cardio-
myopathy.

The results of our study are applicable to
our population with relatively well preserved
ventricular function. In this particular subset,
exercise testing may be able to select patients
who need more aggressive anti-sudden-death
therapy. However, the role of inducibility of
ventricular tachycardia by programmed stim-
ulation and its suppression with antiarrhyth-
imic drugs needs to be assessed relative to
exercise testing in these patients.

1 Podrid PJ, Grabows TB. Exercise stress testing in the man-
agement of cardiac rhythm disorders. Med Clin North
Am 1984;68:1139-44.
2 Callf RM, McKinnis RA, McNeer F, Harrel FE, Lee KL,
3 Pryor DB, et al. Prognostic value of ventricular arrhyth-
miass associated with treadmill exercise testing in patients
studied with cardiac catheterization for suspected ischemic heart disease. J Am Coll Cardiol 1983;2:
3 Prata A. Natural history of chagasic cardiomyopathy. In:
Pan American Health Organization, ed. American try-
4 Manço JC, Gallo L, Godoi RA, Fernandes RG, Amorim
5 De Paola AA, Horowitz LN, Myamoto MH, Pinheiro R,
6 Lopes ER, Chapadeiro E. Morte súbita em área endêmica
7 Jelinek MV, Lown B. Exercise stress testing for exposure
to cardiac arrhythmia. Prog Cardiovasc Dis 1974;16:
8 McHenry PL, Morris SN, Kavalier M, Jordan JW. Compara-
tive study of exercise-induced ventricular arrhythmias in normal subjects and patients with docu-
mented coronary artery disease. Am J Cardiol 1976;37:
9 Goldschlager N, Cake D, Cohn K. Exercise-induced ventricular arrhythmias in patients with coronary artery
disease. Their relation to angiographic findings. Am J
Cardiol 1973;31:434-40.
10 Weiner DA, Levine SR, Klein MD, Ryan TJ. Ventricular
arrhythmias during exercise testing: mechanisms, response to coronary bypass surgery and prog-
11 Pombo JF, Troy BL, Russell RO. Left ventricular volumes
and ejection fraction by echocardiography. Circulation
1971;43:480-90.
12 Sokoloff NM, Spielman SR, Greenspan AM, Rae AP,
Porter RS, Lowenthal DT, et al. Plasma norepinephrine in
exercise-induced ventricular tachycardia. J Am Coll Cardiol
1986;8:11-7.
13 Hellant RH, Pion R, Kabde V, Banka VS. Exercise-related
ventricular complexes in coronary heart disease.
Correlations with ischemia and angiographic severity.
14 McHenry PL, Morris SN, Kavalier M, Jordan JW.
Comparative study of exercise-induced ventricular arrhyth-
miass in normal subjects and patients with docu-
mented coronary artery disease. Am J Cardiol 1976;37:
609-16.
15 Flug JL, Lakatta EG. Prevalence and prognosis of exercise-
induced nonsustained ventricular tachycardia in appar-
16 Manço JC, Gallo L, Godoy RA, Fernandes RG, Amorim
17 Josa D, DeQuattro V, Lee DD, Elkahany U, Palmoro H.
Plasma norepinephrine in Chagas' cardiomyopathy: a marker of progressive dysautonomia. Am Heart J