Journal of the American College of Cardiology
© 2005 by the American College of Cardiology Foundation
Published by Elsevier Inc.

Vol. 46, No. 8, 2005
ISSN 0735-1097/05/$30.00
doi:10.1016/j.jacc.2005.06.067

Myocardial Delayed Enhancement by Magnetic Resonance Imaging in Patients With Chagas' Disease

A Marker of Disease Severity

Carlos E. Rochitte, MD,* Paulo F. Oliveira, MD,* Joalbo M. Andrade, MD,* Bárbara M. Ianni, MD,* José R. Parga, MD,* Luiz F. Ávila, MD,* Roberto Kalil-Filho, MD, FACC,* Charles Mady, MD,* José C. Meneghetti, MD,* João A. C. Lima, MD, FACC,† José A. F. Ramires, MD, FACC*

São Paulo, Brazil; and Baltimore, Maryland

OBJECTIVES We sought to investigate whether myocardial delayed enhancement (MDE) by magnetic resonance imaging (MRI) could quantify myocardial fibrosis (MF) in patients with Chagas' heart disease (CHD), thus defining the severity of the disease.

BACKGROUND Myocardial fibrosis secondary to ischemic disease can be imaged using MDE. Advanced CHD is characterized by progressive MF.

METHODS Fifty-one patients with CHD were enrolled: 15 seropositive asymptomatic participants in the indeterminate phase (IND); 26 patients with known clinical CHD; and 10 patients with known CHD and ventricular tachycardia (VT). Using a 1.5-T MRI system, we acquired left ventricular (LV) short-axis slices using cine-MRI (LV function) and inversion-recovery gradient-echo (MDE).

RESULTS Myocardial fibrosis by MRI was present in 68.6% of all patients, in 20% of IND, 84.6% of CHD, and 100% of VT ($p < 0.001$). Quantified MF increased progressively across disease severity subgroups (0.9 ± 2.3% in IND; 16.0 ± 12.3% in CHD; and 25.4 ± 9.8% in VT, $p < 0.001$) and New York Heart Association functional classes (I: 7.5 ± 9.5%; II: 21.9 ± 13.8%; and III: 25.3 ± 9.9% of LV mass, $p < 0.001$). Left ventricular ejection fraction and MF had significant negative correlation ($r = -0.78$, $p < 0.001$), similar to the segmental MF and function: 4.9 ± 15.1% of MF in normal function, 32.5 ± 32.5% in mildly hypokinetic, 57.8 ± 31.4% in severely hypokinetic, and 72.3 ± 36.2% in akinetic and dyskinetic segments, respectively ($p < 0.001$).

CONCLUSIONS In CHD, MDE by MRI quantifies MF that not only can be detected in the early asymptomatic stages but parallels well-established prognostic factors and provides unique information for clinical disease staging. (J Am Coll Cardiol 2005;46:1553–8) © 2005 by the American College of Cardiology Foundation

Chagas' disease is a chronic disease that is caused by *Trypanosoma cruzi* infection (1), a pathogen that has been afflicting humans for millennia (2). The disease currently affects 4% to 7% of Latin Americans, with 200,000 new cases annually (3). Chagas' heart disease (CHD) is the most serious complication, striking approximately one-third of seropositive individuals and is a main cause of death from heart failure in Latin America.

After infection with *T. cruzi* (4), the asymptomatic phase can last for decades (indeterminate) until unknown triggers initiate disease progression to heart failure and arrhythmias in a subset of patients. Pathologic studies of advanced CHD have shown prominent myocardial fibrosis (MF) (5–7). However, serial in vivo quantification of MF across different stages of Chagas' disease has not been previously performed.

Myocardial delayed enhancement (MDE) by magnetic resonance imaging (MRI) is the best noninvasive method to evaluate MF or necrosis caused by acute, chronic myocardial infarction (8–11) or non-ischemic myocardial disease (12).

From the *Heart Institute (InCor), University of São Paulo Medical School, São Paulo, Brazil, and the †Cardiolgy Division, Department of Medicine, Johns Hopkins University, Baltimore, Maryland. Supported by FAPESP (Fundação de Amparo ã Pesquisa do Estado de São Paulo) Grant 01/04358–0 and the Zerbini Foundation.

Manuscript received January 5, 2005; revised manuscript received May 23, 2005, accepted June 20, 2005.

We hypothesized that MDE quantifies myocardial damage caused by CHD at different stages of disease severity. Our objectives were to evaluate the extent, location, and frequency of MF in Chagas' disease and to determine its relation to established parameters of disease severity.

METHODS

We evaluated 51 seropositive patients for Chagas' disease without history of myocardial infarction and at low risk for coronary artery disease (CAD). All patients signed an InCor-approved consent form. Exclusion criteria were previous infarction or CAD, >2 CAD risk factors, valve disease, and MRI contraindications. We enrolled three subgroups at distinct stages of disease progression (Table 1) based on well-recognized markers of worse prognosis (New York Heart Association [NYHA] functional classification, left ventricular [LV] ejection fraction [LVEF], LV volumes, electrocardiogram abnormalities, and ventricular tachycardia) (4,13–15). They consisted of: 1) an indeterminate group (IND group) of 15 asymptomatic patients without signs of cardiac involvement by CHD with normal echocardiography, MRI, electrocardiogram, and chest X-ray; 2) a CHD group of 26 consecutive patients with known heart involvement by CHD defined as abnormal electrocardio-

Abbreviations and Acronyms

CAD = coronary artery disease
CHD = Chagas' heart disease
IND = indeterminate phase group
LV = left ventricular
LVEF = left ventricular ejection fraction
MDE = myocardial delayed enhancement
MF = myocardial fibrosis
MRI = magnetic resonance imaging
NYHA = New York Heart Association
VT = ventricular tachycardia

gram (typically, right bundle branch block with left anterior hemiblock) and/or LV dysfunction; and 3) a ventricular tachycardia (VT) group comprising 10 patients with known CHD, with previously documented episode of ventricular tachycardia, and with normal coronary angiography. All patients in the VT group underwent coronary angiography and electrophysiologic studies within one year from the MRI study.

Magnetic resonance imaging methods. All patients had MRI examination on 1.5-T GE CV/i System (Wakeusha, Wisconsin). Left ventricular short-axis and long-axis imaging planes were obtained, during an 8- to 15-s breath-hold, by two electrocardiogram-triggered pulse sequences at the same exact locations, allowing precise comparisons between LV function and myocardial structure.

A gradient-echo (steady-state free precession) was used for LV function evaluation, and an inversion-recovery prepared gradient-echo was used for MDE (10 to 20 min after intravenous bolus of 0.2 mmol/kg of gadolinium-based contrast), with the following parameters, respectively: repetition time 3.9/7.1 ms, echo time 1.7/3.1 ms, flip angle 45°/20°, cardiac phases 20/1, views per segment 8/16 to 32, matrix 256 × 128/256 ×192, slice thickness 8/8 mm, gap between slices 2/2 mm and field of view 32 to 38/32 to 38 cm, inversion time none/150 to 250 ms, receiver bandwidth 125/31.25 kHz, number of excitations 1/2, acquisition every heart beat for both.

Data analysis. End-systolic, end-diastolic LV volumes, and LVEF were measured by MASS-plus Analysis software (Leiden, the Netherlands), applying Simpson's method. On the MDE short-axis images, LV mass and total extent of MDE (as percent of LV mass) were measured using

Table 1. Patient Characteristics

	All (n = 51)	IND (n = 15)	CHD (n = 26)	VT (n = 10)	p Value
Male gender	19 (37.3)	2 (13.3)	12 (46.2)	5 (50.0)	0.068*
Age (yrs)	50.4 ± 12.9	46.5 ± 12.0	49.3 ± 12.7	58.9 ± 12.0	0.049†
LVEF (%)	49.0 ± 17.8	65.7 ± 7.5	45.7 ± 16.0	32.3 ± 12.7	<0.001†
ESV (ml/m^2)	43.9 ± 33.8	20.3 ± 7.0	48.3 ± 36.1	68.0 ± 32.0	<0.001‡
EDV (ml/m^2)	77.4 ± 35.8	58.3 ± 14.3	80.7 ± 41.0	97.7 ± 32.2	0.005‡
LV mass (g/m^2)	64.6 ± 23.5	57.5 ± 16.0	61.2 ± 25.5	83.9 ± 18.2	0.005‡
Mean NYHA functional class	1.5 ± 0.6	1.0 ± 0.0	1.5 ± 0.6	2.2 ± 0.6	<0.001‡
NYHA functional class >I	20 (39.2)	0	11 (42.3)	9 (90)	<0.001*
BMI (kg/m^2)	24.1 ± 4.0	24.2 ± 3.4	24.5 ± 4.7	22.8 ± 2.8	0.523‡
Hypertension	1 (2.0)	0	1 (3.9)	0	1.000*
Diabetes	1 (2.0)	0	0	1 (10)	0.196*
Hypercholesterolemia	7 (13.8)	2 (13.3)	3 (11.54)	2 (20.0)	0.864*
Current smoker	1 (2.0)	1 (6.7)	0	0	0.490*
CAD family history	1 (2.0)	0	0	1 (10)	0.196*

Data are expressed as mean ± SD or number (%) for discrete variables. *Fisher's exact test. †One-way analysis of variance (ANOVA). ‡One-way analysis of variance by ranks-Kruskal-Wallis test.

BMI = body mass index; CHD = Chagas' heart disease; EDV = end-diastolic volume; ESV = end-systolic volume; IND = indeterminate; LV = left ventricular; LVEF = left ventricular ejection fraction; NYHA = New York Heart Association; VT = ventricular tachycardia.

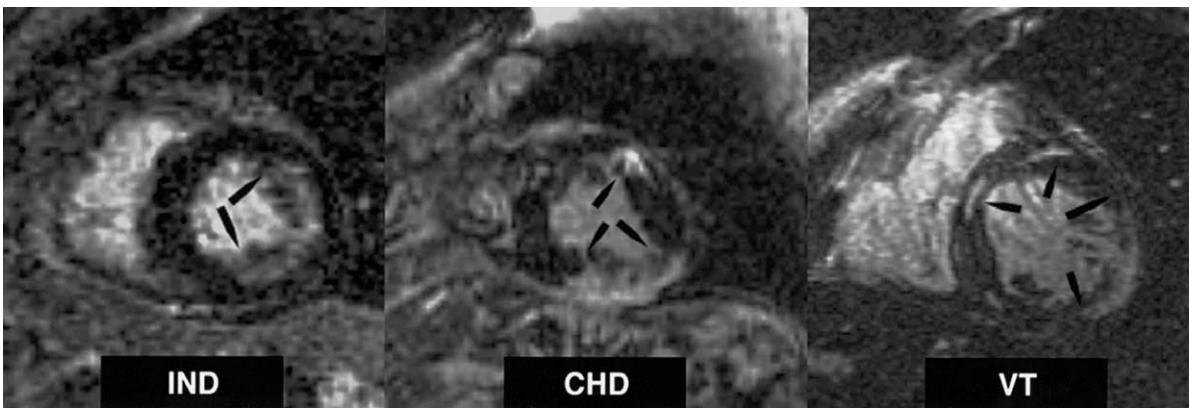

Figure 1. Myocardial delayed enhancement **(arrowheads)** on left ventricular short-axis slices in different stages of Chagas' disease. CHD = Chagas' heart disease group; IND = indeterminate phase group; VT = Chagas' heart disease with ventricular tachycardia group.