Radionuclide Evaluation of Left-Ventricular Function in Chronic Chagas' Cardiomyopathy

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Left-ventricular ejection fraction (LVEF) and abnormalities of regional wall motion (WMA) were studied by means of radionuclide ventriculography in 41 patients prospectively diagnosed as having chronic Chagas' disease. Thirteen patients were asymptomatic (ASY), 16 were arrhythmic (ARR), and 12 had congestive heart failure (CHF). Mean LVEF was normal in ASY (0.64 ± 0.06) but markedly depressed in CHF (0.28 ± 0.08). Regional WMAs were minimal in ASY and their severity increased in ARR. Most CHFs (75%) had diffuse hypokinesia of the left ventricle. The region most frequently affected was the infero-apical (63%). Seven patients had a distinct apical aneurysm. Correlation between radionuclide and contrast ventriculography data was good in 17 patients. For LVEF, r = 0.90. For WMA there was agreement between the two techniques in 77% of 65 segments compared. Best agreement occurred with infero-apical lesions (88%), and worst with septal (69%). Selective coronary arteriography showed normal arteries in all patients. Therefore, chronic Chagas' heart disease joins ischemic heart disease as a cause of regional WMA.

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Chagas' disease is often observed clinically as a chronic cardiomyopathy in South and Central America (*1–3*). A large population—estimated in 1960 to be 10 million—is at risk of infestation with *Trypanosoma cruzi* (*2*). Since serological tests (*4*) allow diagnosis in asymptomatic subjects years before heart disease can be detected clinically, early detection of myocardial damage is of primary importance. Peculiar to this cardiomyopathy is the frequent finding of ventricular apical aneurysm, with localized thinning and fibrosis of adjoining walls (*5–9*).

The present work was undertaken to explore the clinical value of radionuclide ventriculography in the diagnosis of ventricular dysfunction and in assessing wall-motion abnormalities in patients with chronic Chagas' heart disease.

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PATIENTS AND METHODS

The study was carried out in 41 patients prospectively identified for past or present infestation with *T. cruzi* by a positive serum complement-fixation test (Machado-Guerreiro, MG) and a hemaglutinin test, performed and interpreted according to the method of Maekelt (*4*) at the Tropical Medicine Institute of our university. Patients were classified clinically into three groups. The first consisted of 13 asymptomatic (ASY) MG-positive blood donors, eight of them women, whose ages ranged from 34 to 55 yr. The second group consisted of 16 arrhythmic (ARR) patients from the cardiomyopathy clinic, their symptoms being directly related to arrhythmias and not to congestive heart failure. Their ages ranged from 28 to 63 yr, and 10 were women. Fourteen had premature atrial or ventricular contractions and/or episodes of ventricular tachycardia (six patients). Nine patients had single bundle branch or bifascicular block, and one patient had second-degree A-V block. The third

group consisted of 12 patients with congestive heart failure (CHF) in functional Class 3 or 4 (New York Heart Association, NYHA) at their initial examination. Their ages ranged from 40 to 69, and 10 were male. All had two or more of the following symptoms: orthopnea, paroxysmal nocturnal dyspnea, fatigue, cough, and signs of biventricular heart failure such as elevated venous pressure, third heart sound, pulmonary rales, peripheral edema, or congestive hepatomegaly. Atrial and/or ventricular premature extrasystoles occurred in all.

In addition to physical examination conducted independently by two or more observers, all subjects had chest radiographs, 12-lead ECG, and routine laboratory examinations. The clinical, electrocardiographic, and laboratory data were revised and classified by consensus of two or more of the authors. None of the patients had coronary, hypertensive, valvular, or congenital heart disease.

In vivo labeling of erythrocytes was accomplished (*10*) and radionuclide ventriculography (*11,12*) was performed in the 30° right anterior oblique (RAO) or anterior (ANT) projection and also in 40° to 60° left anterior oblique (LAO) projection with a 10° caudal tilt. Computer-generated sixteen-frame images, made up of 600–900 cardiac cycles, were obtained from 60–90% of the cardiac cycle in a 64 × 64 × 8 matrix.

Ejection fraction was determined dividing the stroke counts (end-diastolic minus end-systolic) by the background-corrected end-diastolic counts. Wall-motion abnormalities (WMA) (hypokinesis, akinesis, or dyskinesis) were evaluated from the LAO and RAO or ANT images by dividing the left ventricle (LV) into four regions: anterior (A), septal (S), infero-apical (IA), and postero-lateral (PL). The diagnosis of aneurysm was made when the dyskinetic area was prominent as a systolic bulge at the periphery of the left-ventricular silhouette (*13*).

Seventeen patients underwent contrast angiography and selective coronary arteriography. Left-ventricular ejection fraction was calculated (*14*) and WMAs were evaluated from projected cineangiograms in both the LAO and RAO views.

Ejection fractions calculated from radionuclide data were compared between groups (ASY, ARR, and CHF) by means of the unpaired Student's t-test. A value of $p < 0.05$ was considered statistically significant. Radionuclear and contrast ejection fractions were compared by linear regression. No statistical analysis was attempted for regional wall-motion data.

RESULTS

Radionuclide left-ventricular ejection fractions (LVEF) were highest in the ASY group (0.64 ± 0.06, mean ± s.d.), lower in the ARR group (0.47 ± 0.15), and lowest in the group with CHF (0.28 ± 0.08). The mean differences between groups were statistically significant ($p < 0.001$, Fig. 1). Individually, all patients in the ASY group had normal LVEF (≥0.56), whereas none of the CHF patients had normal LVEF. ARR patients could be separated in two groups (Table 1): those with normal LVEF (8 patients, mean LVEF = 0.60 ± 5.1) and those with abnormal LVEF (8 patients, mean LVEF = 0.34 ± 10.8). Although at the time of initial evaluation they had no clinical signs of CHF, four arrhythmic patients had LVEF below 0.30.

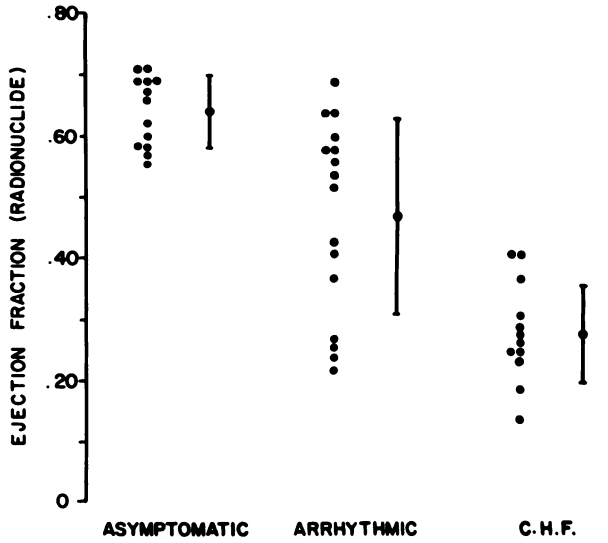

Fig. 1. Left-ventricular ejection fractions in 41 patients with chronic Chagas' disease. Mean differences between three groups were statistically significant ($p < 0.001$).

Analysis of regional wall motion from radionuclide ventriculography data showed distinct segmental involvement (Fig. 2) in 15 patients (37% of the total study group). Fourteen patients had normal wall motion (34%) and 12 patients had diffuse contraction abnormalities (29%). Figure 3 shows the type of regional WMA in each clinical group. In correspondence with the LVEF results, only a small proportion of ASY patients (3/13; 23%) had regional WMA, and none had diffuse ventricular dysfunction, whereas most of the CHF patients (9/12; 75%) had diffuse hypokinesia of the LV.

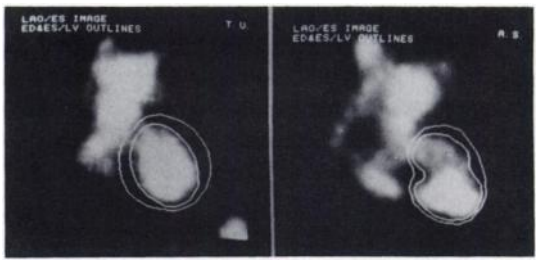

FIG. 2. LAO end-systolic views of radionuclide ventriculograms of two patients with chronic Chagas' cardiomyopathy. Left panel is from a subject with inferoapical hypokinesis; right panel from another patient with extensive inferoapical hypokinesis in addition to systolic dyskinesis of posterolateral and septal regions.

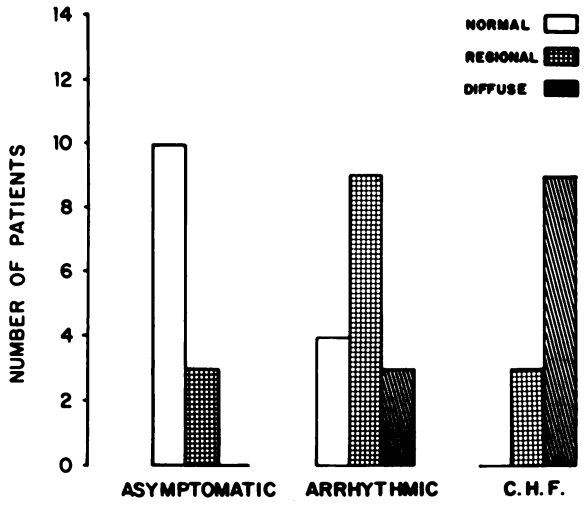

FIG. 3. Left-ventricular wall motion in 41 patients with chronic Chagas' cardiomyopathy of various clinical types.

Normal LVEF was associated with normal wall motion or minimal (one region) WMA. LVEF fell in proportion to the number of regions involved. As mentioned above, ASY and CHF patients were concentrated respectively at the normal and abnormal ends of the LVEF/WMA spectrum. In contrast, ARR patients presented various degrees of LVEF and regional WMA:

TABLE 1. LEFT-VENTRICULAR FUNCTION, REGIONAL WALL MOTION AND ECG ABNORMALITIES IN 16 ARRHYTHMIC PATIENTS WITH CHAGAS' CARDIOMYOPATHY

Patients	LVEF	RWMA	Arrhythmia
1	0.56	0	PACs, PVCs
2	0.54	0	PACs, BBB
3	0.69	0	PVCs
4	0.64	0	PVCs, BBB
5	0.64	IA* (AA)†	PACs, PVCs
6	0.56	IA, (Ant?)‡	PVCs
7	0.58	IA (AA)	PVCs, V. Tach.
8	0.60	IA (AA)	PVCs, BBB
9	0.43	Diff.¶	PACs, PVCs
10	0.22	IA, PL, Ant.	PVCs, BBB
11	0.52	IA (AA)	PVCs, V.Tach., BBB, A-V Block
12	0.24	PL,§ Ant.	PVCs, V.Tach., BBB
13	0.41	IA (AA)	PACs, PVCs, V.Tach.
14	0.27	Diff.	V.Tach., BBB
15	0.26	Diff.	PACs, PVCs
16	0.37	IA (AA)	V.Tach., BBB

* IA = infero-apical region.
† AA = apical aneurism.
‡ Ant. = anterior wall.
§ PL = postero-lateral wall.
¶ Diff. = difusse.

of the 16 patients in this group, four had normal wall motion, six had one abnormal region, one had two abnormal regions, one had three abnormal regions, and three had diffuse abnormalities (Table 1). One ARR patient could not be classified because of technical difficulties. As with the whole patient population, overall ventricular function in ARR patients was related to the severity of regional WMA. Table 1 shows data on the nature of rhythm and conduction disturbances in the patients of this group. There was no apparent correlation between the location and severity of WMA and the type of arrhythmia or conduction disturbance. However, life-threatening ventricular arrhythmias were more frequent in the ARR patients with depressed LVEF.

The region most frequently affected was the IA, which was the site of single contraction abnormality in eight patients and was found in 13 of 15 patients (87%) with segmental involvement. The IA region was the only one affected in ASY patients (3 of 13; 23%, Table 2), the most frequently in ARR patients (11/16; 69%); in the whole series of 41 it was affected in 26 (63%). The S and PL regions were relatively spared in ARR and CHF patients. Seven patients presented a distinct apical aneurysm resulting from akinetic or dyskinetic IA region in an otherwise normally contracting left ventricle. LVEF in patients with apical aneurysm was normal in four subjects and moderately depressed in three.

Selected coronary arteriography showed normal arteries in all patients (no lesion above 50% luminal reduction). The correlation between LVEF calculated from contrast ventriculography and that from radionuclide data was $r = 0.90$ ($y = 0.91x + 3.6$). Regional wall motion was analysed from RAO-60° and LAO-30° contrast ventriculograms, then compared with results obtained independently from radionuclide ventriculograms. Figure 4 illustrates the percentage of agreement in the assessment of normal compared with abnormal regions between the two studies, for a total of 67 segments compared in the 17 patients (ANT segments could not be compared in one patient for lack of radionuclide data). Total agreement was maximal for the IA region (15/17; 88%) and minimal for the septal region (10/17; 59%).

DISCUSSION

Radionuclide ventriculography provided reliable information for global left-ventricular function and regional wall-motion abnormalities in patients with chronic Chagas' heart disease. There was good correlation between contrast and radionuclide ventriculography LVEF ($r = 0.90$). Regional abnormalities of wall motion were also adequately detected by scintigraphic studies. There was complete agreement in the evaluation in 77% of the 67 segments compared by the two techniques. The infero-apical region showed the best agreement (88%) and

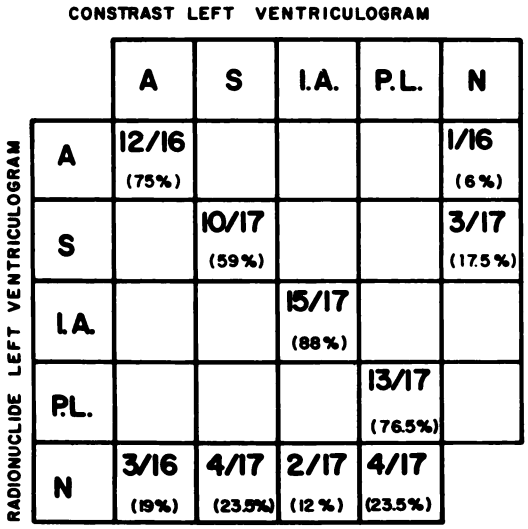

FIG. 4. Correlation between motion of 67 wall segments from 17 patients evaluated by radionuclide and contrast ventriculograms. Figures and percentages along diagonal line correspond to agreement (normal-normal or abnormal-abnormal) for each segment. Values and percentages along edges represent disagreement. A = anterior, S = septum, IA = inferoapical, PL = posterolateral, N = normal.

the septal region the worst (59%). The septal motion was equally understimated (10% of patients) and overstimated (24% of patients) by radionuclide ventriculography. An overall accuracy of 96% has been reported (*15*) for the detection of aneurysms by gated blood-pool scintigraphy. In our study group, three patients who had apical aneurysm were studied by contrast ventriculography, with complete agreement. In two of the cases the diagnosis was later confirmed at the time of surgery.

It should be noted, however, that apical aneurysm is more difficult to identify when generalized hypokinesis is more severe and cardiomegaly is prominent, as in patients with CHF. This may explain in part why most patients with apical aneurysm were in the ARR group.

In selected cases, electrophysiological studies had shown (*16*) ventricular tachycardia due to a re-entry mechanism in the aneurysm. These patients are amenable to aneurysmectomy, which was done in one of our series. Nevertheless, most arrhythmias ensue as part of the cardiomyopathic process.

Our data confirm the previously reported regional myocardial involvement in Chagas' cardiomyopathy (*5,7,9,17-20*). Fifty-six percent (15/27) of the patients who had abnormal LV motion had regional abnormalities. The severity of regional involvement progressed from the asymptomatic to the CHF groups. The region most frequently abnormal was the inferoapical, which was also the only one affected in asymptomatic patients (Table 2). The patterns of regional involvement found in our patients are in agreement with the pathogenic conception of an initial apical lesion that gradually invades other regions until global hypokinesis ensues (*6,9*). These patterns correspond to pathologic observations in autopsy material (*18,19*).

TABLE 2. LEFT-VENTRICULAR REGIONAL WALL MOTION IN DIFFERENT CLINICAL GROUPS OF PATIENTS WITH CHAGAS' CARDIOMYOPATHY

Regions of abnormal wall motion	Clinical groups: Asymptomatic	Arrhythmic	C.H.F.	All patients
Anterior	0/12 (0%)	5/15 (33%)	12/12 (100%)	17/39 (44%)
Septum	0/13 (0%)	3/16 (19%)	10/12 (83%)	13/41 (32%)
Inf.-apical	3/13 (23%)	11/16 (69%)	12/12 (100%)	26/41 (63%)
Post.-lateral	0/13 (0%)	5/16 (31%)	9/12 (75%)	14/41 (34%)

An echocardiographic study (*9*) reported a relative sparing of septal region in Chagas' patients with regional myocardial involvement. In the present study, both the septum and posterolateral wall were less affected (and equally so) than the anterior and inferoapical regions (Table 2). Selective coronary arteriography performed at the time of contrast ventriculography showed normal coronary arteries in all 17 patients. Ten of them had regional WMA in the contrast ventriculogram. Chagas' cardiomyopathy is thus a source of regional WMA and ventricular aneurysms, in addition to coronary artery disease in regions of endemic prevalence. Radionuclide ventriculography WMA are not typical of Chagas' chronic cardiomyopathy; they resemble lesions of coronary artery disease. It is still to be determined whether myocardial perfusion scintigraphy can distinguish the segmental WMA of coronary disease from that of Chagas' origin. At current levels of knowledge, an apical aneurysm with no previous history to suggest ischemia or infarction can be considered throughly suggestive of Chagas' disease in endemic areas.

Left-ventricular ejection fraction was altered in proportion to the number of regions affected by the disease, being normal in the asymptomatic and markedly depressed in CHF patients. Seven arrhythmic patients without clinical evidence of left-ventricular failure, however, had depressed LVEF (mean: 0.34 ± 10.8, Fig. 1). This finding may relate to the relatively frequent discordance between clinical observation and objective evaluation of left-ventricular function (*21,22*).

The present study has shown that radionuclide ventriculography may be useful in the evaluation of patients with chronic Chagas' heart disease. Wall-motion abnormalities and apical aneurysms can be adequately evaluated by cardiac blood-pool scintigraphy. Coronary

and ventricular contrast studies could be performed in those patients on whom coronary heart disease must be ruled out or when aneurysmectomy is considered.

In an ongoing study evaluating the correlation between radionuclide ventriculography and two-dimensional echocardiography, it seems that the latter can detect the apical lesion at an earlier stage. The scintigraphic study appears to provide especially reliable and perhaps more easily reproducible information about ventricular function. In general, it seems that there is good agreement between the two procedures, which complement one another as noninvasive methods, easily accessible and less costly for the patients.

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