Echocardiography in Chagas Heart Disease

Harry Acquatella, MD

Background—Chagas heart disease is a frequent cause of morbidity and mortality in Latin America. Echocardiography provides useful diagnostic and prognostic information and is an important tool in the management of patients with Chagas disease.

Methods and Results—A search for relevant publications was obtained from MEDLINE, LILACS, and SCIELO sources. Acute Chagas myocarditis is a rare disorder in which pericardial effusion is frequent. Echocardiography may exclude pericardial tamponade in case of heart failure. Chronic Chagas cardiomyopathy evolves for several decades after the infection. Epidemiological history, positive serology, and suggestive clinical and ECG abnormalities establish the diagnosis. About three quarters of chronic Chagas cardiomyopathy subjects remain asymptomatic with normal (indeterminate form) or abnormal ECGs. Early Doppler abnormalities includes prolongation of isovolumic contraction and relaxation times. Systolic function frequently is normal, but dysfunction may be elicited by stress tests. Half or more of symptomatic patients have a left ventricular apical aneurysm and other segmental contractile abnormalities similar to those seen in coronary heart disease. The dilated nonsegmental form is indistinguishable from dilated cardiomyopathy. Results from univariate and multivariate Cox survival analyses indicate that impaired systolic function and increased ventricular dimensions have significant value in predicting cardiac morbidity and mortality. Cardiac ultrasound commonly is used in the follow-up of patients and in the assessment of various therapeutic modalities.

Conclusions—Echocardiographic and Doppler techniques provide useful structural and functional information in the detection of early myocardial damage, risk assessment of prognosis, disease progression, and management of patients with Chagas disease. (Circulation. 2007;115:1124-1131.)

Key Words: cardiomyopathy ■ Chagas disease ■ echocardiography, Doppler ■ echocardiography ■ heart failure ■ survival

Chagas disease remains a public health problem in several countries of Latin America. Prophylactic control programs have diminished substantially the number of infected individuals from 16 to 18 million in the early 1990s to 11 million in a recent estimation, but ~100 million persons still continue to be at risk of acquiring the infection.1 The diagnosis of Chagas disease requires an epidemiological history and ≥2 positive serologic tests. Cardiac damage is suspected by ≥1 of the following ECG findings: right bundle-branch block, left anterior fascicular block, AV blocks, multiform ventricular beats, sinus bradycardia, abnormal ST-T segment, and abnormal T and Q waves.2-7 The decreasing prevalence of the disease in some endemic areas or migration of infected subjects to urban nonendemic places within or outside their original country may result in misdiagnosis of a cardiomyopathy of different origin.8,9 Two-dimensional and Doppler echocardiography provides additional valuable information on cardiac structure and function that complements information provided by ECG. This review is focused primarily on the utility of cardiac ultrasound in the diagnosis, classification, and detection of early myocardial damage and the prognostic assessment of patients with Chagas disease. Other aspects of epidemiology and pathophysiology are briefly considered.

Acute Chagas Disease
Chagas disease usually is acquired during childhood.1,3,4,7 Infected forms of Trypanosoma cruzi present in the feces of reduvidae insects penetrate the skin or conjunctiva of people living in poor rural housing. The disease has an acute phase and a chronic phase. Acute Chagas disease may appear as a nonspecific febrile illness lasting for ~2 to 8 weeks, becoming clinically manifest in <1% of infected subjects.3,4 Acute chagasic myocarditis is infrequent, appearing in only 1% to 5% of those having the acute phase (1 to 5 of every 10 000 infected subjects).4 The largest published echocardiographic series on acute Chagas disease includes 58 subjects.10 Abnormal 2-dimensional echocardiograms were present in 52%, and pericardial effusion was seen in 42%. In 10 of 12 patients with heart failure (HF), the effusion was moderate to severe. Of note, mean left ventricular ejection fraction (LVEF) was normal (63%). Apical or anterior dyskinesis was found in 21%, and only 6% had LV dilation. Five patients died, 4 of...
them in HF. In 2 other reports, pericardial effusion was present in 7 of 8 patients, 3 of whom were in tamponade. Figure 1 shows a patient with this complication who improved substantially after pericardiocentesis. These findings demonstrate the need to perform echocardiograms to rule out a rapidly treatable cause of HF (pericardial effusion) and to evaluate systolic dysfunction during the acute phase. More studies are necessary.

Chronic Chagas Disease

In most patients, the initial infection occurs unnoticed, passing to the chronic stage 1 to several decades later. On histology, diffuse and patchy chronic myocarditis, interstitial mononuclear cell infiltrates, and myocardial fiber destruction with fibrotic replacement are commonly present (Figure 2). Most initial autopsy studies performed in subjects dying at the end stage of the disease reported grossly enlarged hearts. A pioneering necropsy work pointed out the high rate of LV chagasic apical aneurysm found in these patients. This result was confirmed by others studies, including a large series of 1078 autopsies in which apical aneurysms were found in ≥ half of cases, more frequently in male than in female patients, and at similar proportions in all age groups. Eighty-two percent were found at the LV apex, 9% at the right ventricular (RV) apex, and 9% at both. Other series had rates ranging from 30% to 92%. Additional LV segmental lesions such as at the posteroinferior walls ranged from 21% to 33% (Figure 2).

Chronic Chagas cardiomyopathy (CCM) may be detected with or without symptoms. Most investigators combine clinical and ECG findings, cardiomegaly, and systolic dysfunc-

| Figure 1. Four-chamber apical view echocardiogram of a woman with a 1-month history of acute Chagas myocarditis with pericardial effusion and tamponade. Chamber size and systolic function were normal. Notice the compression of the right atrial (RA) wall. LA indicates left atria; PE, pericardial effusion. |
| Figure 2. Echocardiogram and postmortem specimen from a patient who had HF secondary to CCM. A, M-mode long-axis, slow-sweep echocardiogram showing the relatively preserved systolic septal (S) motion and thickening and a thin, noncontractile posterior wall (PW). B, Long-axis autopsy section of the heart. Notice the LV apical and posteroapical fibrotic thinning with relative septal sparing. The coronary arteries were normal. Reproduced from Acquatella et al, with permission of the publisher. Copyright © 1980, the American Heart Association. |
mortality (50%) at 2 years. In all groups, coronary angiography, when performed, is normal or shows nonsignificant lesions.

Echocardiographic and Doppler Findings

Anatomic Abnormalities

In asymptomatic subjects, it may be difficult to differentiate precisely a normal thin apical segment from an early scar. This difficulty may explain the different rates of apical abnormalities published in various reports.

LV cavity opacification with ultrasound contrast and harmonic imaging may help in difficult cases. The aneurysm may range from as small as a “hollow punch” to large, indistinguishable from a myocardial infarction.

The mean prevalence of LV aneurysm from different 2-dimensional echocardiographic series was 8.5% (range, 1.6% to 8.6%) among 920 asymptomatic individuals or patients with mild cardiac damage and 55% (range, 47% to 64%) in 242 patients with moderate to severe cardiac impairment (Table 1 and Figure 3). In a recent work that included 1053 subjects, it was less frequent, 2% in subjects with a normal ECG and 24% in those with an abnormal ECG. In logistic regression analysis, the LV apical aneurysm was an independent predictor of mural thrombus. In another work, patients with aneurysms had a significant association with thrombus and stroke during a mean follow-up of 2 years.

Segmental LV contractile abnormalities of other walls also may be detected. The most common is at the posteroinferior wall, with a mean prevalence of 20% (range, 5.3% to 22%) in 1164 asymptomatic subjects or patients with mild heart damage and of 23% (range, 16% to 30%) in 280 patients having symptoms or with HF (Figure 2).

Endocardial curvature and global shape evaluated by Fourier analysis of LV 2-dimensional echocardiograms disclosed a significantly decreased apical curvature with a more spherical LV, resulting in a disruption of the optimal global prolate-ellipsoid shape even in patients with relatively preserved LV volumes. This finding may suggest that early segmental lesions may progress to diffuse hypokinesis and increased LV end-diastolic dimensions as found in advanced disease.

### Table 1. Clinical, ECG, and Echocardiographic Findings in CCM

<table>
<thead>
<tr>
<th>NYHA class</th>
<th>Asymptomatic CCM</th>
<th>Symptomatic CCM</th>
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<tbody>
<tr>
<td></td>
<td>A</td>
<td>B</td>
</tr>
<tr>
<td>ECG</td>
<td>Normal</td>
<td>Abnormal</td>
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<tr>
<td>RBBB, %</td>
<td>-</td>
<td>9–18</td>
</tr>
<tr>
<td>LAFB, %</td>
<td>-</td>
<td>9–15</td>
</tr>
<tr>
<td>PVCs, %</td>
<td>-</td>
<td>3–9</td>
</tr>
<tr>
<td>AVB 1–2, %</td>
<td>-</td>
<td>2–5</td>
</tr>
<tr>
<td>Heart size</td>
<td>Normal</td>
<td>Increased</td>
</tr>
<tr>
<td>LV aneurysm, %</td>
<td>1.6–8.6</td>
<td>47–64</td>
</tr>
<tr>
<td>LV posterobasal lesion, %</td>
<td>5.3–22</td>
<td>16–30</td>
</tr>
<tr>
<td>LV ejection fraction</td>
<td>Normal</td>
<td>Decreased</td>
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<tr>
<td>LV diastolic function*</td>
<td>NL</td>
<td>NL, PR</td>
</tr>
<tr>
<td>Survival at 5 y, %</td>
<td>~98</td>
<td>~85</td>
</tr>
</tbody>
</table>

RBBB indicates right bundle-branch block; LAFB, left anterior fascicular block; PVCs, premature ventricular contractions; AVB 1–2, first- and second-degree AV block; NL, normal; PR, prolonged relaxation; PN, pseudonormal; RR, restrictive reversible; and RI, restrictive irreversible. Percentages represent the range of means from different series.

*All may have prolonged isovolumic times.

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**Figure 3.** Two-dimensional 4-chamber echocardiogram apical view of a patient with CCM with an LV apical aneurysm (AA). There is a distinct limit between the normal contractile myocardium and the dyskinetic apex (arrows). LVEF was moderately decreased (~40%).
Subjects presenting with the indeterminate form almost invariably have a normal global systolic function, but some may have abnormal echocardiograms. Among 505 subjects with normal ECGs and a mean normal LVEF of 67%, 13% had segmental lesions and 0.8% had systolic dysfunction. In contrast, of 257 persons with abnormal ECGs and a mean LVEF of 68%, 33% had segmental lesions and 8% had systolic dysfunction. Both groups had normal biventricular end-diastolic and end-systolic dimensions.\(^{31}\) In patients with abnormal ECGs, global systolic function has prognostic implications. A cohort of 538 patients\(^ {39}\) grouped in 4 stages of disease progression (A to D)\(^ {24}\) had markedly dissimilar 5-year survival rates of 98%, 91%, 45%, and 13% for those with a normal LVEF, mildly decreased LVEF, reversible HF, or irreversible HF, respectively.

With tissue Doppler imaging (TDI), myocardial velocity systolic shortening and diastolic lengthening (E’ and A’) during the cardiac cycle can be estimated (Figure 4). With TDI, subjects with normal ECGs and 2-dimensional echocardiograms have shown prolonged LV\(^ {41,42}\) and RV\(^ {43}\) isovolumic contraction times as signs of early contractile abnormalities. Thus, a normal ECG does not rule out myocardial

**Figure 4.** Doppler findings of the patient in Figure 3 (tracings are aligned with the first QRS complex). A, Mitral valve pulsed-wave Doppler displays a decreased E/A ratio of 0.64 and a prolonged E deceleration time of 295 ms, consistent with a diastolic pattern of prolonged relaxation. Mitral regurgitation was mild. B, TDI at the septal mitral annular level shows prolonged isovolumic contraction time (ICT) and relaxation time (IRT) of 130 and 155 ms, respectively. S, E’, and A’ peak velocities are decreased. Note the prominent apical-directed IRT wave (white arrow on C), probably related to earlier relaxation of the aneurysm. C, Color Doppler M-mode velocity propagation of the LV inflow tract. A diminished slope of the color edge in early diastole (white line) represents a lower velocity of blood flow toward the aneurysmal apex, consistent with loss of apical suction.
abnormalities, the clinical significance of which is currently unknown.

In patients with normal EF, systolic dysfunction may become apparent under pharmacological stress. An impairment for chronotropic, global, and regional contractile responses has been seen during standard dobutamine stress echocardiography. Some patients show a biphasic response (initially augmentation followed by hypocontractility at higher dobutamine doses) predominantly at the LV posteroinferior wall segments, suggestive of viable but dysfunctional myocardium. The possible mechanisms are complex and may include β-adrenergic dysfunction, endothelial dysfunction, ischemia, and structural myocardial damage. Others have shown a lower slope of the end-systolic pressure–dimension relation during phenylephrine infusion, suggestive of a reduction in LV contractility in patients with the indeterminate form, mild cardiac involvement, or the digestive form of the disease.

RV systolic impairment may be the only abnormality detected by biventricular radionuclide angiography. In contrast, in a recent group of 74 patients studied by 2-dimensional and Doppler echocardiography, RV dysfunction, when present, was secondary to the severity of LV damage and high levels of pulmonary pressure rather than primary RV depressed function. These apparently discordant results may be due to the different techniques used.

Diastolic Function
The chronic myocarditic damage may impair ventricular relaxation and diastolic filling. Diastolic abnormalities usually precede systolic dysfunction. Reduced LV compliance leads to an increase in left atrial pressure, changes in transmural and pulmonary venous flow velocities, and prolongation of systolic and diastolic time intervals. Early works using simultaneous M-mode echocardiographic, phonocardiographic, and apex cardiographic tracings had already shown that significant prolongation of the isovolumic relaxation and ventricular filling times was present in asymptomatic subjects with normal systolic function and in symptomatic patients.

The combination of pulsed Doppler of mitral valve inflow, pulmonary veins, and mitral annular TDI velocities currently is used to classify patients into 4 groups of worsening diastolic function: abnormal relaxation, pseudonormal, reversible, and nonreversible restrictive filling. In a group of 169 CCM subjects, diastolic dysfunction was found in ≈20% of the patients. There was a strong correlation between worsening diastolic function and increased left atrial and ventricular dimensions and decreased LVEF. A reduced TDI septal E’ wave of 11 cm/s and a septal E/E’ ratio of >7.2 were highly sensitive and moderately specific and had a high negative predictive value for detecting any kind of diastolic dysfunction (Figure 4). Another group of 89 patients were classified according to the presence of normal or pseudonormal ventricular filling pattern. Patients

<table>
<thead>
<tr>
<th>Author</th>
<th>Patients, n</th>
<th>Mean Follow-Up, mo</th>
<th>Mortality, %</th>
<th>Mortality Predictors*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ianni et al</td>
<td>159</td>
<td>99</td>
<td>0</td>
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<tr>
<td>Viotti et al</td>
<td>849</td>
<td>118</td>
<td>0.6</td>
<td>... ... ... LVSD, LVEF, group</td>
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<tr>
<td>Salles et al</td>
<td>738</td>
<td>58</td>
<td>8</td>
<td>74 22 4</td>
</tr>
<tr>
<td>Xavier et al</td>
<td>1053</td>
<td>66</td>
<td>10</td>
<td>57 22 4</td>
</tr>
<tr>
<td>Bestetti et al</td>
<td>56</td>
<td>24</td>
<td>28</td>
<td>69 31 6</td>
</tr>
<tr>
<td>Rodriguez-Salas et al</td>
<td>283</td>
<td>48</td>
<td>38</td>
<td>37 44 6</td>
</tr>
<tr>
<td>Mady et al</td>
<td>104</td>
<td>30</td>
<td>48</td>
<td>64 36 6</td>
</tr>
</tbody>
</table>

SD indicates sudden death; EM, embolism; LVSD, left ventricular systolic dimension; Group, clinical group of each series; QTd, ECG QT-interval dispersion; FS, fractional shortening; and EPSS, M-mode echocardiographic E-point septal separation. Decimals were rounded.

*Multivariate analysis.

Figure 5. Inverse significant correlation between LVEF and mortality among 3138 patients from 6 echocardiographic series. The first letter indicates the author initial; the second, the group. I indicates Ianni et al; V, Viotti et al; S, Salles et al; B, Bestetti et al; R, Rodriguez-Salas et al; Mady et al; Y, yes; N, no. See text and Table 2 for other details.
with pseudonormal filling pattern had statistically significantly larger LV dimensions, higher LV wall motion score, and lower LVEF. TDI was able to differentiate CCM patients with normal LV diastolic function from those with a pseudonormal filling pattern and increased LV filling pressures.

**Other Echocardiographic Doppler Techniques**

In color M-mode, early inflow jet velocities across the mitral valve as it moves toward the apex display a slope representing the blood flow velocity propagation\(^{40}\) (Figure 4). A group of CCM patients had decreased velocity propagation consistent with relaxation abnormalities, which was more pronounced in those with LV apical aneurysm. LVEF and pulsed-wave Doppler patterns were not significantly different between CCM patients and a control group.\(^{53}\)

The myocardial performance index (Tei index) is a global function index combining the time duration of systole and diastole by pulsed-wave Doppler.\(^{54}\) A study found abnormally high values of LV myocardial performance index (\(\geq 0.32\)) in one third of asymptomatic subjects, in all of symptomatic patients, and in 2% of the control subjects.\(^{55}\) ECG abnormalities in the asymptomatic chagasic patients were associated with abnormal myocardial performance index, but not in the control subjects with the same ECG changes. Symptomatic patients had markedly increased RV and LV myocardial performance index values, suggestive of severe myocardial dysfunction.

Doppler-derived myocardial strain also has been studied in patients with Chagas disease.\(^{56}\) CCM patients had lower radial and longitudinal values compared with normal control subjects. However, strain was not able to differentiate between normal control subjects and subjects with the indeterminate form of the disease. This technique was able to quantify subtle segmental contractile dysfunction not detected visually.

**Echocardiographic Prognostic Variables**

Echocardiographic series of chronic CCM patients were selected on the basis of having survival analysis performed by the Cox multivariate method (Table 2 and Figure 5). The populations included subjects with a broad expression of disease severity ranging from none\(^{31,38}\) to none to severe\(^ {31,32,34,57,58}\) to severe symptoms.\(^ {59,60}\)

No mortality occurred in 2 series of asymptomatic subjects with normal ECG at entry. In 1 series of 159 subjects, there were no events.\(^{38}\) LVEF remained normal in all subjects, and ECG was unchanged in nearly 80%. In the other series of 505 subjects, 8% had events.\(^{31}\) In the same work, among 257 asymptomatic subjects with an initially abnormal ECG, mortality was 1%, and 26% had clinical events. In 87 patients with abnormal ECGs\(^ {31}\) and cardiomegaly but no HF, 52% had clinical events with 14% mortality. On multivariate analysis, change in clinical group, LV systolic dimension, and LVEF were predictors of mortality. Chagas-related ECG abnormalities, LV diastolic and systolic dimensions, and LVEF were predictors of events.\(^ {31}\)

Four series included mixed populations, from asymptomatic subjects to patients with HF. One consisted of 738 patients.\(^{57,58}\) QT-interval dispersion and LV end-systolic dimension were the strongest independent predictors of all end points. In another work of 1053 subjects classified according to whether an LV apical aneurysm was present,\(^ {34}\) LVEF remained the only significant predictor of mortality. Apical aneurysm was not significant when adjusted for LVEF. In a study of 283 patients\(^ {32}\) grouped as asymptomatic and symptomatic, significant mortality risk factors were initial NYHA class, E-point septal separation, and M-mode echo fractional shortening. Finally, 2 series had patients with severe HF. One collected 56 persons in NYHA functional classes III and IV.\(^ {59}\) The only significant risk factor was LVEF. In a series of 104 male patients\(^ {60}\) in NYHA functional classes II, III, and IV, statistically significant differences between survivors and nonsurvivors on multivariate analysis were LVEF and maximal \(\text{O}_2\) uptake (\(\text{VO}_2\text{max}\)). Thus, systolic dysfunction and increasing heart size emerged as significant predictors of morbidity and mortality (Figure 5).

**Applications in the Management of Patients**

Echocardiography is used in the routine clinical evaluation of CCM patients to assess disease progression, in survival studies\(^{31,32,34,38,57–60}\) to rule out the presence of intraventricular thrombus,\(^ {29,34}\) in the follow-up of pacemakers devices\(^ {61}\) and implanted automatic cardioverter-defibrillators,\(^ {62}\) and to monitor response to vasodilator therapy in patients with HF (enalapril)\(^ {63}\) or to antiparasitic medications (benznidazole),\(^ {64}\) among others. The last study showed in a long-term follow-up that the only independent predictors of deteriorating clinical status were a lower echocardiographic LVEF and a higher LV end-diastolic diameter.

**Study Limitations**

The echocardiographic and Doppler findings of CCM are nonspecific and may be similar to those observed in other cardiomyopathies (ischemic and nonischemic). A need exists for comparative studies to estimate the sensitivity and specificity of such abnormalities. The prognostic value of associated mitral regurgitation or RV dysfunction is unknown. LVEF should be preferentially estimated by 2-dimensional instead of M-mode echocardiography because the latter does not evaluate the frequently abnormal ventricular apex of these patients.

**Conclusions**

In patients with acute chagasic myocarditis, echocardiograms should be performed almost routinely, especially if HF is present, to exclude pericardial effusion and tamponade. In the chronic phase, subjects with a normal ECG have a good long-term prognosis; most have normal global systolic function, but contractile and diastolic abnormalities may be found, although the significance of these findings in disease progression is unknown. Ventricular involvement in CCM symptomatic individuals may range from an isolated small LV apical aneurysm to a globally dilated heart without segmental scars. A chagasic origin should be considered in the differential diagnosis of a cardiomyopathy patient with a positive epidemiological history and serology, suggestive ECG abnormalities, and apical aneurysm. Depressed LVEF and increased LV internal dimensions emerged in different survival studies.
as significant risk factors associated with increasing morbidity and mortality.

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Disclosures

None.

References


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