Electrocardiogram in Chagas disease

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Abstract

Since the initial descriptions of Chagas cardiomyopathy (ChCM), the electrocardiography has played a key role in patient evaluations. The diagnostic criterion of chronic ChCM is the presence of characteristic electrocardiographic (ECG) abnormalities in seropositive individuals, regardless of the presence of symptoms. However, these ECG abnormalities are rarely specific to ChCM and, particularly among the elderly, can be caused by other simultaneous cardiomyopathies. ECG abnormalities can predict the occurrence of heart failure, stroke, and even death. Nevertheless, most prognostic studies have included Chagas disease (ChD) populations and, not exclusively, ChCM. Thus, more studies are required to evaluate the efficacy of ECG in predicting reliable prognoses in established chronic ChCM. This review exclusively discusses the role of the 12-lead ECG in the clinical evaluation of chronic ChD.


INTRODUCTION

Since the initial descriptions of Chagas cardiomyopathy (ChCM), electrocardiography has played a key role in patient evaluations. Chagas and Villela considered arrhythmia the predominant symptom of ChCM. Although there are many unclear aspects of Chagas disease (ChD), the electrocardiography is a well-known method to diagnose and define ChD prognoses. Moreover, it is a low-cost and widely used examination even in remote areas.

The diagnostic criterion of chronic ChCM is the presence of characteristic ECG abnormalities in seropositive individuals, regardless of the presence of symptoms. Chronic ChCM is the most severe and frequent form of ChD and affects 20% to 40% of all patients with chronic ChD. During the course of the disease, the ECG shows progressive abnormalities that indicate worsening myocardial damage. Maguire et al. demonstrated that 20% of patients with ChD developed cardiac abnormalities within 6 years, while abnormalities were detected in only 10% of the seronegative individuals. Recently, a study reported a cardiomyopathy incidence of 1.85 per 100 people-years. Chronic ChCM presents as three basic syndromes, heart failure, cardiac arrhythmia, and thromboembolism, which can occur concomitantly in a patient. The clinical presentation varies widely according to the disease duration and extent of myocardial damage.

This review exclusively discusses the role of the 12-lead ECG in the clinical evaluation of chronic ChD.

SEARCH METHOD

Data for the present review were identified through a search of the PubMed and Lilacs databases using the following Medical Subject Headings (MeSH) terms: Chagas Cardiomyopathy OR Chagas Disease AND Electrocardiogram*. The search was performed in February 2018 and considered all studies conducted with human adults published in English, Portuguese, or Spanish. There were no restrictions with respect to sample size or duration of follow-up. The original search identified 576 articles. However, after reading the titles and abstracts of the original articles to find any and all terms related to ECG alterations and 12-lead ECG, only 120 were selected for complete reading of the text. After reading the text of the selected studies, only 49 articles met the criteria for this investigation. To describe the relationship between ChD and stroke, a new search was conducted using the following MeSH terms: Chagas Cardiomyopathy OR Chagas Disease AND Stroke. This search identified 140 studies. However, after reading the titles and abstracts of the original articles to find any and all terms related to ECG alterations and 12-lead ECG, only seven met the inclusion criteria.

PREVALENCE OF ELECTROCARDIOGRAPHIC ALTERATIONS

ECG abnormalities were more prevalent in the patients with ChD than in the seronegative patients, and this has been consistently demonstrated in many studies. A retrospective observational study assessed 264,324 primary-care patients including 7,590 self-reported patients with ChD. Only 31.4%
of patients with ChD had a normal ECG versus 61.1% of the seronegative patients. In addition, having a higher prevalence of an abnormal ECG, patients with ChD also presented with more abnormalities per tracing, and the proportion of those with more than three alterations reached nearly 20%.[7,14] Although the number of ECG alterations naturally increases with age, the increase is more pronounced in patients with ChD.[7,15] Maguire et al.[10], upon examining a rural-area population, also identified that an abnormal ECG is more frequent in patients who are seropositive for ChD, and the ECG abnormalities are more remarkable in those patients between 25 and 44 years of age. The authors also showed that ECG abnormalities are more frequent in men than in women (26.1% vs 15.3%).[10] This same research group described the progressive nature of ECG alterations during a 6-year follow-up that showed the incidence of ECG abnormalities was higher in patients who were ChD seropositive, and no new abnormalities were found in the elderly.

The progressive nature of ECG alterations in the elderly is controversial and needs to be clarified. In an elderly cohort with a mean age of 68 years, 86.9% of patients with ChD had ECG abnormalities compared to 75.8% of the seronegative patients (p < 0.001). These findings indicate that only a small proportion of elderly patients with ChD present the indeterminate form of ChD, contrary to that reported in previous studies. The higher prevalence of ECG abnormalities in ChD seropositive patients indicates that the abnormalities are not only explained by other cardiopathies, but also by ChCM progression. It was further demonstrated that ECG alterations and their associations are related to a higher risk of death in elderly patients with ChD. This may be due to the continuous process of cardiac damage beginning with the infection in childhood and continuing throughout the patients’ entire adulthood. This leads to a higher frequency of ECG abnormalities, which is an established cardiomyopathy marker in infected elderly patients compared to non-infected patients.

ChD can cause any type of ECG alteration, but conduction disturbances and ventricular extra systoles (VES) are the most common. ChD seems to evolve from a normal ECG, then to mild alterations, and then to defined characteristic abnormalities. Thus, after some initial nonspecific alterations, there is a tendency for more complex ECG abnormalities to occur.[6,16,17] Nearly 8% of all patients with ChD experience a regression in ECG alterations, particularly those related to ventricular depolarization and repolarization, and VES.[18,19] However, the disappearance of ECG abnormalities must be viewed as a consequence of ECG mutability and not as a true regression.[18,19]

It is important to consider that the presence of nonspecific, isolated ECG alterations are frequently found in both patients with ChD and healthy persons, and include sinus bradycardia (heart rate ≥ 40bpm), first degree atrioventricular block, nonspecific ventricular repolarization (VR) alterations, QRS axis deviation from 0 degree through -30 degree, low limb voltage, isolated supraventricular and ventricular premature beats, incomplete right bundle branch block, and isolated left anterior hemiblock. Thus, these ECG alterations should not be considered diagnostic criteria of ChCM.[2]

The prevalence of each ECG abnormality depends on the studied population and is shown in Table 1, which describes the results from observational studies that evaluated more than 200 patients with ChD. In Table 1, right bundle branch block (RBBB) associated with left anterior hemiblock (LAH) cases are not included in the RBBB count unless they are signalized. Given that most of the studies are Brazilian and that Rosenbaum[20] was a pioneer in ChD studies, we chose to include his work in the Table 1 despite the use of a population of less than 200 patients with ChD. Many studies have shown a remarkable prevalence of RBBB[10,11,16,20-22] and its strong association with ChD.[10,15] Marcolino et al. found an odds ratio (OR) of 10.73 [95% confidence interval (CI) 10.10–11.41] that improved when RBBB was combined with LAH (OR: 12.09, 95% CI 11.20–13.04). The combination of RBBB and LAH (Figure 1) was more prevalent in ChD than in other cardiomyopathies.[21,23] Despite the low frequency in ChD,[24] left bundle branch block (LBBB) is markedly associated with heart failure.

Patients with ChCM have a longer PR interval[10,14,15] and QRS complex duration[14,15] compared to seronegative patients. Moreover, as a consequence of conduction disturbances, ChCM has a strong association with pacemaker (PM) rhythm (OR: 13.29, 95% CI 11.47–15.40), and second degree (OR: 4.05, 95% CI 2.47–6.63) and third degree (OR: 13.29, 95% CI 11.47-5.40) atrioventricular block (AVB).[7]

The presence of electrical inactivity (EI), whether isolated or combined with other alterations on the ECG, was associated with ChCM.[22,25] Its prevalence ranges from 0.5% to 30% among the studies in the literature. EIs are often associated with ventricular conduction disturbances and VES,[10,22] which could indicate more extensive myocardial damage and a worse survival rate.[26,27]

Ventricular repolarization (VR) abnormalities are quite frequent[13,14], and the prevalence ranges from 0.2% to 40%.[28] These abnormalities tend to occur during the early course of the disease[28] before the occurrence of other abnormalities and are not related to a worse prognosis.[29] Prata et al. considered VR abnormalities nonspecific,[13] since they could be a consequence of diffuse myocarditis,[28] autonomic dysfunction, or even malnourishment.[13] Although VR alterations and EIs are usually associated with coronary artery disease, the patients with ChCM had normal coronary arteries.[30,31] Moreover, the ischemia shown in the patients’ scintigraphy was not associated with ECG alterations, thoracic pain,[30,31] or severe wall-motion abnormalities at rest.[31]

Atrial fibrillation (AF) is often associated with ChD (OR: 3.15, 95% CI 2.83-3.51), and its prevalence is higher in the elderly[2,13] and in men.[7] The prevalence of AF in ChD is similar to the other cardiomyopathies[23]. Thus, this arrhythmia is more indicative of a worse prognosis than of a specific alteration.[14]

VES is a high-frequency abnormality,[13,22,24] and is associated with a worse prognosis[17]. However, the 12-lead ECG does not recognize the transitory character of this ventricular arrhythmia nor does it allow for the evaluation of its severity.[26]. This alteration can also occur in the ECG of healthy people and cannot differentiate patients who are ChD seropositive from those who are seronegative. Although VES is typical of ChCM, it should not be considered specific.[26]
### TABLE 1: Prevalence of electrocardiographic alterations in Chagas disease patients in the studies.

<table>
<thead>
<tr>
<th>Author (year)</th>
<th>Number sample</th>
<th>Mean age</th>
<th>RBBB</th>
<th>RBBB + LAH</th>
<th>LBBB</th>
<th>VR</th>
<th>EI</th>
<th>VES</th>
<th>AF/Flutter</th>
<th>PM</th>
<th>AVB 1&lt;sup&gt;st&lt;/sup&gt; or 2&lt;sup&gt;nd&lt;/sup&gt;</th>
<th>AVB 3&lt;sup&gt;rd&lt;/sup&gt;</th>
<th>LV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rosenbaum &amp; Alvarez, 1955&lt;sup&gt;a&lt;/sup&gt;</td>
<td>130 (H)</td>
<td>47</td>
<td>48.4</td>
<td>-</td>
<td>2.3</td>
<td>37.0</td>
<td>-</td>
<td>47.0</td>
<td>14.6</td>
<td>-</td>
<td>6.1</td>
<td>3.8</td>
<td>13.0</td>
</tr>
<tr>
<td>Laranja et al, 1956&lt;sup&gt;b&lt;/sup&gt;</td>
<td>683 (P)</td>
<td>-</td>
<td>48.3</td>
<td>-</td>
<td>2.2</td>
<td>12.9</td>
<td>-</td>
<td>42.6</td>
<td>6.6</td>
<td>-</td>
<td>28.1</td>
<td>8.2</td>
<td>-</td>
</tr>
<tr>
<td>Dias &amp; Kloetzel, 1968&lt;sup&gt;b&lt;/sup&gt;</td>
<td>387 (P)</td>
<td>-</td>
<td>11.3</td>
<td>-</td>
<td>0.5</td>
<td>4.9</td>
<td>-</td>
<td>17.0</td>
<td>1.8</td>
<td>-</td>
<td>2.8</td>
<td>2.6</td>
<td>-</td>
</tr>
<tr>
<td>Maguire et al, 1983&lt;sup&gt;c&lt;/sup&gt;</td>
<td>346 (P)</td>
<td>-</td>
<td>5.8</td>
<td>4.6</td>
<td>9.0</td>
<td>0.6</td>
<td>7.5</td>
<td>-</td>
<td>-</td>
<td>1.4</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Arteaga et al, 1985&lt;sup&gt;d&lt;/sup&gt;</td>
<td>553 (H)</td>
<td>46</td>
<td>10.6</td>
<td>25.3</td>
<td>2.3</td>
<td>30.9</td>
<td>30.7</td>
<td>18.8</td>
<td>4.4</td>
<td>-</td>
<td>5.5</td>
<td>11.2</td>
<td>-</td>
</tr>
<tr>
<td>Pereira &amp; Coura, 1986&lt;sup&gt;e&lt;/sup&gt;</td>
<td>255 (P)</td>
<td>-</td>
<td>18.4</td>
<td>-</td>
<td>-</td>
<td>18.0</td>
<td>5.5</td>
<td>14.5</td>
<td>1.2</td>
<td>6.6</td>
<td>-</td>
<td>2.7</td>
<td></td>
</tr>
<tr>
<td>Acquatella et al, 1987&lt;sup&gt;f&lt;/sup&gt;</td>
<td>775 (P)</td>
<td>47.7</td>
<td>16.7</td>
<td>-</td>
<td>0.7</td>
<td>19.6</td>
<td>5.9</td>
<td>20.1</td>
<td>3.8</td>
<td>-</td>
<td>4.2</td>
<td>0.5</td>
<td>-</td>
</tr>
<tr>
<td>Barreto et al, 1989&lt;sup&gt;g&lt;/sup&gt;</td>
<td>1,004 (O)</td>
<td>41.5</td>
<td>40.7</td>
<td>-</td>
<td>2.0</td>
<td>40.4</td>
<td>38.5</td>
<td>29.0</td>
<td>4.2</td>
<td>-</td>
<td>10.4</td>
<td>5.6</td>
<td>-</td>
</tr>
<tr>
<td>Prata et al, 1993&lt;sup&gt;h&lt;/sup&gt;</td>
<td>2,000 (O)</td>
<td>45.5</td>
<td>32.4</td>
<td>-</td>
<td>1.9</td>
<td>28.2</td>
<td>7.1</td>
<td>42.2</td>
<td>9.0</td>
<td>-</td>
<td>10.8</td>
<td>3.9</td>
<td>1.2</td>
</tr>
<tr>
<td>Garzon et al, 1995&lt;sup&gt;i&lt;/sup&gt;</td>
<td>1,010 (O)</td>
<td>-</td>
<td>33.3</td>
<td>-</td>
<td>3.1</td>
<td>26.7</td>
<td>25.1</td>
<td>40.3</td>
<td>2.5</td>
<td>-</td>
<td>6.0</td>
<td>5.6</td>
<td>7.0</td>
</tr>
<tr>
<td>Salles et al, 2003&lt;sup&gt;j&lt;/sup&gt;</td>
<td>738 (O)</td>
<td>46.3</td>
<td>14.1</td>
<td>24.3</td>
<td>3.3</td>
<td>7.7</td>
<td>3.7</td>
<td>14.5</td>
<td>-</td>
<td>-</td>
<td>6.5</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Rassi et al, 2006&lt;sup&gt;k&lt;/sup&gt;</td>
<td>424 (H)</td>
<td>47</td>
<td>18.6</td>
<td>24.3</td>
<td>7.1</td>
<td>27.8</td>
<td>6.6</td>
<td>37.3</td>
<td>3.1</td>
<td>-</td>
<td>9.0</td>
<td>-</td>
<td>9.0</td>
</tr>
<tr>
<td>Williams-Blangero et al, 2007&lt;sup&gt;l&lt;/sup&gt;</td>
<td>722 (P)</td>
<td>41.9</td>
<td>15.2</td>
<td>5.2</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>0.7</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
</tbody>
</table>

RBBB: right bundle branch block; LAH: left anterior hemiblock; LBBB: left bundle branch block; VR: ventricular repolarization; EI: electrical inactivity; VES: ventricular extra systoles; AF: atrial fibrillation; PM: pacemaker rhythm; AVB 1<sup>st</sup>: first degree atrioventricular block; AVB 2<sup>nd</sup>: second degree atrioventricular block; AVB 3<sup>rd</sup>: first degree atrioventricular block; LV: low voltage; H: hospitalized; O: outpatient; P: population. *Cases are included in the RBBB count.
ELECTROCARDIOGRAPHIC ALTERATIONS RELATED TO HEART FAILURE

The ECG of patients with ChD can show valuable information about a patient’s evolution to heart failure (HF). The main studies that evaluated this aspect are described in Table 2. In patients with ChD, there is a significant correlation between a QRS duration > 100ms and a reduced left ventricle ejection fraction (LVEF) and increased dimensions of the left ventricle in diastole. However, QRS duration does not correlate to regional abnormalities of left ventricle contraction or the presence of apical aneurisms; hence, QRS cannot predict a normal left ventricle. The importance of QRS duration in this cross-sectional study is corroborated by an 8-year follow-up cohort that identified QRS duration as the only isolated electrocardiographic variable that correlated with a drop of 5% or more in the LVEF and an increase in the diameter of the left ventricle in diastole. The appearance of new ECG abnormalities also correlated to a drop in the LVEF.

Ribeiro et al. reinforced this finding in 2013 when they reported that a QRS duration > 120ms and a QT interval > 440ms can predict with moderate accuracy a reduced LVEF in patients with ChD. This same study also identified the abnormalities most frequently associated with LVEF in ChD: frequent supraventricular premature beats, VES, AF, RBBB, possible old myocardial infarction, and major isolated ST-T wave abnormalities. These results corroborate with the findings of Barreto et al. who identified a higher incidence of ECG abnormalities in ChCM populations in heart-failure classes III and IV (New York Heart Association), including VES (p < 0.001), ventricular conduction disturbances (p < 0.001), EI (p < 0.001), and VR alterations (p < 0.001). The combination of ventricular conduction disturbances with VES or with sinus bradyarrhythmia was associated with both, reduced LVEF and increased left ventricle diameter.

The QRS score estimates the fibrosis area by considering the alterations of amplitude, duration, and morphology of Q, R, and S waves. Each point corresponds to an area of 3% fibrosis in the left ventricle. A QRS score > 2 points had the highest accuracy for predicting the presence of any late gadolinium enhancement and reduced LVEF in cardiac resonance.

ELECTROCARDIOGRAPHIC ALTERATIONS RELATED TO STROKE RISK IN CHAGAS DISEASE

ChD is an independent risk factor for stroke incidence, even when compared to a high-risk population for this outcome and an OR of 7.17 (95% CI 1.50-34.19) may be associated with it. Furthermore, elderly patients with ChD who have had a stroke have a higher risk of death than the seronegative patients. An evaluation of death due to a stroke in ChD using the Cox model identified that AF is a variable with a higher hazard ratio (HR): 3.87 (95% CI 1.26-11.91), followed by B-type natriuretic peptide. Although AF is an important risk factor in the genesis of ischemic stroke related to ChD, one study showed that the occurrence of AF was not associated with stroke in patients with ChCM, while there was an association with the presence of LV thrombus and apical aneurysm. These results could be a consequence of the study’s cross-sectional character, and the protection provided by anticoagulation.

Sousa et al. elaborated on a score to evaluate thromboembolic risk in ChD. These authors identified several independent risk variables: left ventricle (LV) systolic dysfunction (HR: 13.21, 95% CI 4.72-37), apical aneurysm (HR: 2.32), LV thrombus (HR: 2.62, 95% CI 1.20-5.7) on the 12-lead ECG. Another study illustrated that the incidence of stroke is higher in patients with mild LV dysfunction (mean LVEF of 48%) compared to those with severe dysfunction (mean LVEF of 36%) and there was no association with the presence of thrombus in the left atrium. This reinforces the role of ECG abnormalities as predictors of stroke.

ELECTROCARDIOGRAPHIC ALTERATIONS RELATED TO DEATH RISK IN CHAGAS DISEASE

The main causes of death in ChD are HF, sudden death, and stroke, with a predominance of HF and stroke. Although the majority of patients show clinical evidence of HF before sudden death, almost one-third of these events occur in asymptomatic individuals who seldom have normal clinical and radiographic exams and who rarely have normal ECGs. ECG carries important information about mortality that must be analyzed in the clinical exam. Table 3 summarizes the studies that showed ECG alterations related to the risk of death.

FIGURE 1: An electrocardiogram showing the typical features of Chagas cardiomyopathy. It displays right bundle branch block associated with left anterior hemiblock.
TABLE 2: Electrocardiographic alterations related to heart failure in Chagas disease patients.

<table>
<thead>
<tr>
<th>Author (year)</th>
<th>Number</th>
<th>Population</th>
<th>End points</th>
<th>Follow up</th>
<th>Prognostic factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cohort studies</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pereira et al, 198518</td>
<td>248</td>
<td>ChD vs Seronegatives</td>
<td>Progression to HF</td>
<td>6 years</td>
<td>EI, VR, VES incidence</td>
</tr>
<tr>
<td>Acquatella et al, 198755</td>
<td>775</td>
<td>With and without cardiomyopathy</td>
<td>Functional class (NYHA)</td>
<td>5 years</td>
<td>Abnormal ECG</td>
</tr>
<tr>
<td>Barretto et al, 198927</td>
<td>1,004</td>
<td>ChD</td>
<td>Functional class (NYHA), cardiothoracic index</td>
<td>2 years</td>
<td>Higher incidence of abnormal ECG in NYHA III and IV.</td>
</tr>
<tr>
<td>Ianni et al, 20015</td>
<td>159</td>
<td>ChD indeterminate form</td>
<td>LVEF</td>
<td>98.6 +/- 30.4 months</td>
<td>Incidence of new ECG alterations had no impact on LVEF</td>
</tr>
<tr>
<td>Nascimento et al, 201233</td>
<td>152</td>
<td>With and without cardiomyopathy</td>
<td>Drop of 5% of LVEF, diameter of the left ventricle in diastole</td>
<td>6.8 years</td>
<td>QRS duration and appearance of new ECG alterations.</td>
</tr>
<tr>
<td>Cross-sectional studies</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Casado et al., 199034</td>
<td>44</td>
<td>ChCM without HF</td>
<td>LVEF, left ventricle volume</td>
<td>Cross-sectional</td>
<td>Association of ECG alterations in the same tracing.</td>
</tr>
<tr>
<td>Ribeiro et al., 200032</td>
<td>98</td>
<td>With and without cardiomyopathy</td>
<td>LVEF, Diameter of the left ventricle in diastole</td>
<td>Cross-sectional</td>
<td>QRS &gt; 100ms.</td>
</tr>
<tr>
<td>Salles et al., 200334</td>
<td>738</td>
<td>With and without cardiomyopathy</td>
<td>LVEF</td>
<td>Cross-sectional</td>
<td>QTd &gt; 60ms,</td>
</tr>
<tr>
<td>Marques et al., 200635</td>
<td>106</td>
<td>Asymptomatic chronic ChD</td>
<td>Diastolic and systolic dysfunction</td>
<td>Cross-sectional</td>
<td>Presence of typical ECG alterations</td>
</tr>
<tr>
<td>Strauss et al., 201135</td>
<td>44</td>
<td>With and without cardiomyopathy</td>
<td>Late gadolinium enhancement area, reduced LVEF</td>
<td>Cross-sectional</td>
<td>QRS score</td>
</tr>
<tr>
<td>Ribeiro et al., 201334</td>
<td>1,000</td>
<td>With and without cardiomyopathy</td>
<td>LVEF</td>
<td>Cross-sectional</td>
<td>QTc interval, QRS duration.</td>
</tr>
</tbody>
</table>

ChD: Chagas disease; HF: heart failure; EI: electrical inactivity; VR: ventricular repolarization; VES: ventricular extra systoles; NYHA: New York Heart Association; ECG: electrocardiographic; LVEF: left ventricular ejection fraction; ChCM: Chagas cardiomyopathy; QTd: QT dispersion; QTc: corrected QT interval.

Patients with normal ECGs have a life expectancy compatible with their gender and age4,43, while those with ECG abnormalities have a higher mortality rate4,43 even if there is no other sign of HF50. The mortality rate increases when an individual with an altered ECG develops HF.

Patients with combined ECG alterations have a higher mortality rate28, and the presence of three or more alterations indicates a poor prognosis. There has been a preponderance of sudden death in patients who had VES with RBBB or primary T-wave alterations. However, when RBBB is associated with VR alterations, a death caused by HF was more common28. The number of alterations in the ECG was also a predictor of death in one cohort of patients with ChCM8. In this cohort, the combination of RBBB and LAH was most heavily related to death8, which corroborates with other studies27,46-48.

Altersations of P, QRS, and T-axes represent a risk of death: (HR: 1.48, 95% CI 1.16-1.88), (HR: 1.34, 95% CI 1.04-1.73), and (HR: 1.35, 95% CI 1.07-1.71), respectively28. T-wave axis deviations (> -15° to > -180° or > 105° to < 180°) were also associated with death in another study28. A wider QT interval was related to death and was possibly a determining factor of sudden arrhythmic death41. This same study identified that EI was a prognostic variable41, which corroborated with the findings of a previous study27.

The analysis of the only cohort comprised solely of patients with ChCM was published in 200628. The final model indicated that only one 12-lead ECG variable, low QRS voltage (LV) (HR: 1.87, 95% CI 1.03-3.37), increased the risk of death. It must be highlighted that LV did not predict adverse outcomes in other cohorts. It is possible that the ECG alterations important to the prognosis of patients with ChD as a whole, do not have the same prognostic value in those with established cardiomyopathy.

CONCLUSIONS

Electrocardiographic abnormalities are frequent in ChD and indicate the presence of cardiomyopathy. However, they are not specific for ChD and, particularly among the elderly, can be caused by other simultaneous cardiomyopathies.

ECG abnormalities can predict the occurrence of HF, stroke, and death. Nevertheless, most prognostic studies have included ChD populations, but not exclusively ChCM. Thus, more studies are needed to evaluate the prognostic value of ECG in established chronic ChCM.
### TABLE 3: Electrocardiographic alterations related to death in Chagas disease patients.

<table>
<thead>
<tr>
<th>Author (year)</th>
<th>Number</th>
<th>Population</th>
<th>Follow up</th>
<th>Prognostic factors</th>
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<tbody>
<tr>
<td>Porto, 1964&lt;sup&gt;39&lt;/sup&gt;</td>
<td>503</td>
<td>With and without cardiomyopathy</td>
<td>5 years</td>
<td>VES, number of ECG alterations</td>
</tr>
<tr>
<td>Espinosa et al, 1985&lt;sup&gt;56&lt;/sup&gt;</td>
<td>107</td>
<td>With and without cardiomyopathy</td>
<td>10 years</td>
<td>ECG alterations, HF symptoms</td>
</tr>
<tr>
<td>Acquatella et al, 1987&lt;sup&gt;73&lt;/sup&gt;</td>
<td>775</td>
<td>With and without cardiomyopathy</td>
<td>5 years</td>
<td>ECG alterations, functional class</td>
</tr>
<tr>
<td>Maguire et al, 1987&lt;sup&gt;4&lt;/sup&gt;</td>
<td>1,017</td>
<td>ChD vs Seronegatives</td>
<td>7 years</td>
<td>Incidence of ECG alterations</td>
</tr>
<tr>
<td>Barreto et al, 1989&lt;sup&gt;77&lt;/sup&gt;</td>
<td>1,004</td>
<td>ChD</td>
<td>2 years</td>
<td>Higher incidence of VES and IE</td>
</tr>
<tr>
<td>Espinosa et al, 1991&lt;sup&gt;58&lt;/sup&gt;</td>
<td>66</td>
<td>With and without cardiomyopathy</td>
<td>12 years</td>
<td>AF</td>
</tr>
<tr>
<td>Bestetti et al, 1993&lt;sup&gt;46&lt;/sup&gt;</td>
<td>24</td>
<td>ChD who had sudden death</td>
<td>Case control</td>
<td>ECG alterations (VES 79%; LAH 58%; RBBB 37%; VR alterations 41%; Ei 25%; AVB 14%; AF 16%)</td>
</tr>
<tr>
<td>Salles et al, 2003&lt;sup&gt;31&lt;/sup&gt;</td>
<td>738</td>
<td>With and without cardiomyopathy</td>
<td>58 +/- 39 months</td>
<td>EI, QTd &gt; 65ms increments; QTc Bazet &gt; 465ms</td>
</tr>
<tr>
<td>Salles et al, 2004&lt;sup&gt;53&lt;/sup&gt;</td>
<td>738</td>
<td>With and without cardiomyopathy</td>
<td>58 +/- 39 months</td>
<td>T-axis deviation (&gt; -15° to &gt; -180° or &gt; 105° to &lt; 180°)</td>
</tr>
<tr>
<td>Viotti et al, 2005&lt;sup&gt;47&lt;/sup&gt;</td>
<td>856</td>
<td>ChD with cardiomyopathy without HF and ChD without cardiomyopathy</td>
<td>8 years</td>
<td>Intraventricular conduction disturbances; ventricular tachycardia</td>
</tr>
<tr>
<td>Rassi et al, 2006&lt;sup&gt;52&lt;/sup&gt;</td>
<td>424</td>
<td>ChD with cardiomyopathy</td>
<td>7.9 +/- 3.2 years</td>
<td>LV of QRS</td>
</tr>
<tr>
<td>Gonçalves et al, 2010&lt;sup&gt;46&lt;/sup&gt;</td>
<td>120</td>
<td>ChD</td>
<td>24 years</td>
<td>RBBB + LAH, LBBB, Polymorphic ventricular tachycardia, PR interval &gt; 0.16 s.</td>
</tr>
<tr>
<td>Ribeiro et al, 2014&lt;sup&gt;4&lt;/sup&gt;</td>
<td>1,462</td>
<td>Elderly with and without cardiomyopathy</td>
<td>10 years</td>
<td>Presence and number of major ECG alterations (Minnesota code); RBBB + LAH was the most important alteration.</td>
</tr>
<tr>
<td>Moraes et al, 2018&lt;sup&gt;60&lt;/sup&gt;</td>
<td>1,426</td>
<td>General population (38% with ChD)</td>
<td>12.8 years</td>
<td>Abnormal axis of P, QRS, and T waves.</td>
</tr>
</tbody>
</table>

**VES**: ventricular extra systoles; **ECG**: electrocardiogram; **HF**: heart failure; **ChD**: Chagas disease; **AF**: atrial fibrillation; **LAH**: left anterior hemiblock; **RBBB**: right bundle branch block; **VR**: ventricular repolarization; **EI**: electrical inactivity; **AVB**: atrioventricular block; **QTd**: QT interval dispersion; **QTc**: corrected QT interval; **LV**: low voltage; **QRS**: QRS wave; **LBBB**: Left bundle branch block; **PR**: PR interval; **P**: P wave.

**Conflict of interest**
The authors declare that there is no conflict of interest.

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