Profile of Chagasic Patients with Implantable Cardioverter Defibrillators (ICD)

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Abstract

**Background:** Sudden death accounts for 55-65% of the deaths from Chagas disease, and the implantable cardioverter-defibrillator (ICD) is the most effective therapy to prevent sudden death in patients with ventricular tachyarrhythmias.

**Objective:** To describe the clinical profile of patients with chronic Chagas disease with ICD admitted to a referral hospital.

**Methods:** 75 chagasic patients with ICD, admitted to Santa Casa de Misericórdia de Goiânia, from January 2011 to December 2013, were evaluated by means of medical record review.

**Results:** The sample (n=75) was composed of 57 (76.0%) male patients and 18 (24.0%) female patients. Clinical admissions accounted for 60.0% of the sample, while surgical ones accounted for 40.0%. Out of all clinical admissions, 40 (89.0%) were due to heart problems: heart failure (HF), with 13 (32.0%) patients, and electrical storm (ES), with 12 (30.0%) patients. Out of the 30 surgical admissions, 17 (56.66%) were due to battery depletion.

**Conclusion:** The clinical profile of patients with chronic Chagas disease with CDI is characterized as follows: male, aged 51-60, presence of dual-chamber devices, appropriate use of antiarrhythmic drugs and beta-blockers, presence of systemic hypertension (SH), left ventricular ejection fraction (LVEF) of 35-45%, clinical admissions due to heart problems (particularly HF and ES), and zero to three post-implantation admissions.

**Keywords:** Implantable defibrillators; Sudden death; Chagas disease; Cardiac arrhythmias

Introduction

Heart involvement is the most important and severe manifestation in the chronic phase of Chagas disease (ChD). This complication occurs in all endemic areas in proportions ranging from 10-40% of HIV-positive individuals, and manifests itself from five to 30 years after primary infection¹².

Tissue changes caused by the infectious and inflammatory process confirm clinical manifestations of chronic Chagas cardiopathy (CCC). Progressive destruction of the heart tissue leads to changes in the electrical bundles of the heart and consequent cardiac conduction disorders, clinically manifesting itself as potentially life-threatening cardiac arrhythmias³. Sudden death is one of the most significant phenomena of the natural history of Chagas disease, accounting for 55-65% of deaths; the often found mechanism is the sustained ventricular tachycardia (SVT), degenerating into ventricular fibrillation (VF).

The therapeutic armoury in the fight against sudden death includes antiarrhythmic drugs, endocardial catheter ablation and the implantation of electronic...
ABBREVIATIONS AND ACRONYMS

- CCC – chronic Chagas cardiopathy
- ICD – implantable cardioverter defibrillator
- DM – diabetes mellitus
- COPD – chronic obstructive pulmonary disease
- CKD – chronic kidney disease
- AF – atrial fibrillation
- LVEF – left ventricular ejection fraction
- VF – ventricular fibrillation
- SH – systemic hypertension
- HF – heart failure
- NYHA – New York Heart Association
- ES – electrical storm
- SVT – sustained ventricular tachycardia

International studies reveal a high readmission rate for individuals with ICD and the extent to which this phenomenon adversely impacts on the patients’ quality of life. It is necessary to better understand both variables involved and determining factors for hospitalization so that strategies can be planned in order to prevent/reduce them, reduce morbidity and mortality and improve the quality of life of post-implanted patients. The scarce production in this line of research is also noticeable in regional and national hospitals, which elicits the need for this study to be developed. This study aims to describe the clinical characteristics of chagasic patients with ICD, who are hospitalized for clinical and/or surgical treatment of possible complications.

In this period, there were 138 hospitalizations of patients with CDI from which 75 were selected for the study. The study included patients older than 18 years, seropositive chagasic patients with ICD, patients with completed medical records and patients who have undergone implant surgery at SCMG. Hospitalization was determined to be the stay in hospital for a period longer than 12 hours after the device implantation.

Data were collected from electronic and handwritten medical records. The following variables were analyzed: gender, place of birth, age, origin, reason for installation of ICD, implantation date, number and reasons for post-implantation interventions, the current reason for hospitalization, drugs currently in use, medical procedure used in current hospitalization, left ventricular ejection fraction (LVEF), device brand and models, associated morbidities, use of resynchronization therapy, electronic evaluation and outcomes.

Data found were tabulated by calculation of percentages, tables and graphs built by 2007 Microsoft Excel programs. As the study is not analytical, results were not analyzed by means of specific methods.

Results

75 patients were included in the study: 57 (76.0%) males and 18 (24.0%) females. The predominant age group was 51-60 years old (n=30; 40.0%) and the arithmetic mean age was 61.86 (Table 1).

Device manufacturers found were: Medtronic, in 40 (53.33%) patients; Biotronik, in 33 (44.0%) patients and St. Jude Medical, in 2 (2.66%) patients. The most commonly installed models were Lumax 340 DR-T (Biotronik), accounting for 26 (34.66%) installed devices, followed by Virtuoso II (Medtronic), accounting for 22 (29.33%). Dual-chamber ICDs were found in 64 (85.33%) patients and single-chamber devices were found in 11 (14.67%) patients. Biventricular stimulation was found in 13 (17.33%) patients.

Regarding the time period since implantation, 12 (16.0%) patients had undergone implantation from zero to six months earlier, followed by 12 (16.0%) patients, with approximately 72 months; 11 (15.0%) patients, with up to 24 months; 10 (13.0%), with 48 months; 8 (11.0%), with up to 12 months; 8 (11.0%), with 36 months; 7 (9.0%) patients, with 60 months, and 7 (9.0%) patients with over 72 months.

Methods

Descriptive study conducted by means of review of medical records of chagasic patients with ICD, admitted to Santa Casa de Misericórdia de Goiânia (SCMG), from January 2011 to December 2013 according to inclusion criteria.

The study was approved by the Research Ethics Committee of Universidade Federal do Rio de Janeiro, in accordance to Brazilian National Health Council Resolution (CNS) no. 466/12.
Device implantation was indicated based upon patients’ clinical manifestations: 27 (36.0%) patients due to spontaneous tachyarrhythmias detected by Holter or electrocardiogram (ECG); 27 (36.0%) patients diagnosed by electrophysiology study and 21 (28.0%) patients who resuscitated after having received CRP.

As for drugs used by patients: 58 (77.33%) were being treated with a combination of antiarrhythmic drugs and beta-blockers; 11 (14.67%) patients were taking antiarrhythmic drugs only; 3 (4.0%) were taking two antiarrhythmic drugs and beta-blockers and 3 (4.0%) were being treated with beta-blockers only.

Among the morbidities found, SH was the most prevalent, being found in 22 (29.33%) patients; smoking habits and/or regular alcohol consumption: 21 (28.0%) patients; CHF: 20 (26.66%) patients; hypothyroidism: 9 (12.0%) patients; chronic obstructive pulmonary disease (COPD): 7 (9.33%) patients; chronic kidney disease (CKD): 7 (9.33%) patients; atrial fibrillation: 8 (10.66%) patients; diabetes mellitus: 6 (8.0%) patients, and the digestive form of Chagas disease: 6 (8.0%) patients.

Regarding LVEF, 24 (32.0%) patients had rates <35%; 29 (38.67%) had rates ranging from 35 to 45%, and 22 (29.33%) patients had rates > 45% (Table 1).

As for hospitalizations, 75 (86.66%) patients had zero to three hospitalizations before the latest admission; 9 (12.0%) patients had three to six hospitalizations, and only 1 (1.33%) had more than six hospitalizations before the latest admission (Table 1). The reasons for the current admission were: 45 (60.0%) patients were admitted due to clinical reasons, and 30 (40.0%) due to surgical reasons.

In this study, 30.0% of clinical cardiac hospitalizations were due to electrical storm resulting from ventricular tachycardia (VT), with no possible identification of the triggering factors. All cases included a treatment based on adjusting antiarrhythmic drugs, with amiodarone impregnation, use of beta-blockers, sedatives, and infusion of cell membrane stabilizer (magnesium sulphate); 2 (16.66%) cases required radiofrequency ablation, whereas the other 2 (16.66%) only required device to be reset associated with drug-based treatment.

40 (88.88%) hospital admissions out of those for clinical reasons (n=45) were secondary to cardiac abnormalities, being 13 (32.0%) due to decompensated HF; 12 (30.0%) due to ES; 7 (17.5%) due to appropriate shocks; 4 (10.0%) due to device failure to deliver therapy, and 4 (10.0%) secondary to phantom shocks (Figure 1). The remaining clinical admissions (n=5, 11.11%) were secondary to non-cardiac reasons, due to the following causes: 1 (20.0%) due to COPD; 1 (20.0%) due to erysipelas; 1 (20.0%) due to pneumonia; 1 (20.0%) due to cerebrovascular accident (CVA), and 1 (20.0%) due to seizure.

### Table 1
Clinical characteristics of patients

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Patients</th>
<th>%</th>
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<tbody>
<tr>
<td>Age group</td>
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</tr>
<tr>
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</tr>
<tr>
<td>41-50</td>
<td>8</td>
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<td>61-70</td>
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<tr>
<td>≥71</td>
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<td>24.00</td>
</tr>
<tr>
<td>Gender</td>
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<td></td>
</tr>
<tr>
<td>Female</td>
<td>18</td>
<td>24.00</td>
</tr>
<tr>
<td>Male</td>
<td>57</td>
<td>76.00</td>
</tr>
<tr>
<td>Left ventricular ejection fraction</td>
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<td></td>
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<tr>
<td>≤ 35%</td>
<td>24</td>
<td>32.00</td>
</tr>
<tr>
<td>&gt; 35% and ≤ 45%</td>
<td>29</td>
<td>38.67</td>
</tr>
<tr>
<td>&gt; 45%</td>
<td>22</td>
<td>29.33</td>
</tr>
<tr>
<td>Number of previous hospital admissions</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-3</td>
<td>65</td>
<td>87.00</td>
</tr>
<tr>
<td>&gt;3 and &lt;6</td>
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<td>12.00</td>
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<tr>
<td>&gt;6</td>
<td>1</td>
<td>1.00</td>
</tr>
<tr>
<td>SH</td>
<td>22</td>
<td>29.33</td>
</tr>
<tr>
<td>Hypothyroidism</td>
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<td>12.00</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
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<td>8.00</td>
</tr>
<tr>
<td>Digestive form of Chagas disease</td>
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<tr>
<td>Atrial fibrillation</td>
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</tr>
<tr>
<td>Chronic heart failure</td>
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<td>26.66</td>
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<tr>
<td>Smoking/drinking</td>
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<td>28.00</td>
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<td>COPD</td>
<td>7</td>
<td>9.33</td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>7</td>
<td>9.33</td>
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</table>

SH - systemic hypertension; COPD - chronic obstructive pulmonary disease
17 (56.66%) hospital admissions out of those for surgical reasons (n=30) were due to battery depletion. The remaining ones were due to device settings and/or repair: 3 (10.0%) were due to increase in the shock electrode threshold; 2 (6.66%) due to electrode breaking; 2 (6.66%) due to electrode displacement; 2 (6.66%) due to implantation of the third electrode in the left ventricle; 2 (6.66%) due to increase in the shock electrode impedance (Figure 2).

As for treatment, 37 (49.33%) patients received medicinal treatment; 3 (4.0%) patients received clinical treatment and ablation; 1 (1.33%) patient had the device reset and received ablation; 4 patients (5.33%) received clinical treatment and had the device reset.

30 (40.0%) patients received surgical treatment. From among surgical procedures, 18 (60.0%) received a new generator; 5 (16.66%) had the electrodes repositioned; 4 (13.33%) received new generators and electrodes; 2 (6.66%) had shock electrodes replaced with new ones, and 1 (3.33%) received a new electrode for resynchronization (Figure 3).

As for the outcome, 66 (88.0%) patients were discharged with clinical improvement and 9 (12.0%) died: 3 due to decompensated HF; 3 due to ES; 1 due to appropriate shocks secondary to SVT; 1 due to pneumonia, and 1 patient was readmitted due to low shock impedance.

Discussion

Seventy-six percent of the patients studied were male: a result similar to that observed in a research based on 1,609 Danish records of patients with CDI. The authors pointed out the male gender as a risk factor for appropriate shocks and inappropriate therapies, although they did not find any possible explanations for this characteristic.

Antiarrhythmic drugs alter cardioversion and defibrillation thresholds, which may influence shock impacts on the myocardium. In this study, 58 (77.33%) patients were being treated with a combination of antiarrhythmic drugs and beta-blockers. The OPTIC study, in which 412 patients with CDI were randomly sampled for therapies using beta-blockers, combined amiodarone and beta-blocker or sotalol therapy alone, revealed that within a one-year follow-up period, amiodarone and beta-blocker combined was the most effective therapy to reduce ICD shocks. The incidence of shocks in the beta-blocker group was 38.5%; 24.3% in the sotalol group, and 10.3% in the combined amiodarone/beta-blocker group.
LVEF is an important parameter to predict hospital readmission, as well as the functional classification of the New York Heart Association (NYHA). In relation to this parameter, 29 (38.67%) patients, from among 35-45%, had LVEF, followed by 24 (32.0%) patients with rates < 35%, and 22 (29.33%) patients with rates > 45%. These numbers were expected, as decompensated heart failure was the leading clinical cause of hospital admissions, accounting for 32.5% of the clinical readmissions.

This factor was assessed in another study7 that monitored 133 patients with CDI, from 1999 to 2003. The authors found that the average number of hospitalizations unrelated to arrhythmia was significantly higher in patients suffering from LVEF: <30% (p=0.019). Functional class III patients had a cardiac-related hospitalization rate higher than those in NYHA class I or II (p=0.010 and p=0.038, respectively). The authors found no correlation between time for the first hospitalization and age, LVEF or NYHA functional class. Only LVEF <30% behaved as an independent risk factor for readmissions unrelated to arrhythmia.

In a study10 conducted in 2013, a correlation was found between LVEF and risk for ICD-delivered therapies and mortality. The authors noticed that patients with LVEF <25% were at increased risk of inappropriate therapy, which is also associated with a higher mortality rate as compared to patients with LVEF ≥25% and patients aged ≥65.

In this study, 17% of patients had a third electrode in the left ventricle for resynchronization. This is in line with data published in a large study12 that discusses the importance of biventricular stimulation in order to improve the quality of life of patients included in NYHA functional class III and IV. The authors reiterate that biventricular stimulation devices can become the best option as first implantation in patients with broadened QRS complex, i.e., ≥140 ms.

In this study, the most prevalent associated morbidities included: SH, found in 22 (29.33%) patients; HF, in 20 (26.66%) patients; smoking habits and/or regular alcohol consumption, in 21 (28.0%) patients; hypothyroidism, in 9 (12.0%) patients; COPD, in 7 (9.33%) patients; CKD, in 7 (9.33%) patients; AF, in 8 (10.66%) patients; DM, in 6 (8.0%) patients, and the digestive form of Chagas disease, in 6 (8.0%) patients. The data obtained are indicative of association between clinical conditions and mortality, since both HF and AF are risk factors for hospital readmissions and for both appropriate and inappropriate ICD-delivered therapies as well. Some authors13 showed an association between increased mortality after appropriate shocks and clinical conditions: urea > 25 mg/dL, absence of beta-blockers, advanced NYHA functional class, presence of AF and DM.

In this study, most hospitalizations (60.0%) were secondary to clinical complications and 40.0% were due to surgical reasons. Regarding clinical hospitalizations, those due to cardiac reasons are the most prevalent, accounting for 88.88% of hospital admissions, being HF the leading cause (32.5%), followed by ES (30.0%); appropriate shocks (17.5%), device failure to deliver therapy (10.0%), and secondary to phantom shocks (10.0%). A similarity is observed between the data obtained in the research and the findings published in the literature7,a which demonstrates that cardiac complications are the leading cause of hospitalization in patients with ICD.

Regarding surgical hospitalizations, the following are the leading causes: battery depletion (57.0%), increase in the shock electrode threshold (10.0%); electrode breaking (7.0%); electrode displacement (7.0%); implantation of the third electrode in the left ventricle (7.0%), and increase in shock electrode impedance (7.0%). It is noteworthy that all patients with electrode breaking had inappropriate shocks as clinical manifestation. It can be seen that the leading cause of surgical readmission was secondary to battery depletion. The research1 also found similar values in 19.0% of readmissions secondary to battery depletion. About 60.0% of failures of epicardial electrodes are asymptomatic and diagnosed either by failure in defibrillation after spontaneous or induced VT or by the abnormalities shown on radiographs evidencing electrode breaking12.

Approximately 85.0% of the patients studied here are patients with dual-chamber ICD. A recent study10 showed a twofold increase in the risk of shocks and inappropriate therapies associated with dual-chamber ICDs, as compared to single-chamber ICDs. Conversely, the literature9 mentions a multicentric study in which comparison was made between single-chamber and dual-chamber detection algorithms. In that study, SVT occurred frequently (34.0% of patients) within six months after ICD implantation. Devices with single-chamber discriminators were found to have improperly classified 40.0% of the SVT episodes. On the other hand, dual-chamber discriminators showed to have caused a significant reduction in the inappropriate detection rate, by 31.0%, and ICD shocks by half.
Another study\(^4\) also points out dual-chamber systems as a potential manner to reduce the incidence of readmission in patients who require chronic stimulation.

During analysis of 148 patients with CDI, by using multivariate Cox regression model, a study\(^4\) showed that the only independent predictor of inappropriate shock was the atrial fibrillation history, and significant univariate predictors of mortality were age ≥70 and LVEF <40%. However, a research found that in addition to atrial fibrillation, information such as smoking history, occurrence of an appropriate shock and high diastolic blood pressure at the measurement moment (≥80 mmHg) are predictors of inappropriate shock\(^5\).

In this study, 17.5% of clinical hospitalizations occurred after appropriate shocks, i.e., patients had VT and ICD delivered the appropriate therapy; 10% of hospitalizations were secondary to shock-free VT, i.e., device failure to deliver the therapy. A similar topic was addressed in another study\(^7\) conducted in 2006, in which authors studied 133 patients with ICD and concluded that sustained ventricular tachyarrhythmia with appropriate therapy accounted for 30.0% of hospital readmissions, whereas ICD failure to deliver therapy accounted for 2%. It is therefore clear that authors found a higher hospitalization rate due to appropriate therapies for this study, and treatment failure rates were slightly higher in this study, accounting for 5.33% of all hospital readmissions.

The importance of a modern and individualized device setting has already been announced by several studies. The use of various antitachycardia pacing (ATP) therapies before shock application has reduced shock and mortality incidence, as compared to conventional setting by using a shock-only ICD therapy. These observations were confirmed by the MADIT-RIT (Multicenter Automatic Defibrillator Implantation Trial Reduce Inappropriate Therapy) study, which observed reduction in both inappropriate shocks (80.0%) and mortality (55.0%) rates caused by the resetting of the device.\(^7\) The authors\(^7\) report about the ease of access to ICD implantation for primary prevention of sudden death in Denmark and, since January 2007, the use of ICD for primary prevention is offered to all patients with left ventricular dysfunction and ischemic heart disease. In Brazil, by contrast, CDI implants for primary prevention are not yet authorized nor provided by the Department of Health/Brazilian Unified Healthcare System (SUS), except for by large hospitals. The major challenge faced in Brazil and worldwide is to find more accurate stratification methods associated with cheaper and all the more durable CDI devices, in order to increase the number of people benefited from a reasonable cost-effectiveness ratio\(^8\).

ES was present in 30.0% of clinical admissions and in 16.0% of all admissions. This syndrome increases the risk of death within the three subsequent months by more than fivefold.\(^13\) For patients who either fail to respond to pharmacological control or remain in incessant VT, endocardial catheter ablation becomes an effective therapeutic measure, as demonstrated in a study\(^11\) that evaluated hemodynamically stable patients with only one VT morphology registered; the acute success rate after ablation was 74.0%, and within the two-year average follow-up period, 80.0% of patients were clinically free from VT recurrence. Within a one-year follow-up period, the monthly frequency of shocks, after successful ablation, decreased from 60 by 0.1. In cases of treatment failure after the use of antiarrhythmic drugs and catheter ablation, patients can benefit from resynchronization therapy with either the left ventricular assistance device or heart transplantation.

As for the outcome, 66 (88.0%) patients were discharged with clinical improvement and 9 (12.0%) died.

Patients in whom HF is the leading clinical cause for hospital admissions, associated with shock development, the long-term monitoring should involve close surveillance throughout the following year of signs and symptoms of imminent decompensated HF. During this time period, special monitoring of recurrent AF (particularly in patients who received inappropriate shocks), as well as titration of antiarrhythmic drugs and beta-blockers to determine the correct dosage, should be performed. Poor prognosis after shocks justifies aggressive surveillance of these patients, including a combination of more frequent clinical encounters, adjustment to HF treatment, in addition to periodic inspections of the device.

The descriptive method used limited this study to the extent that it did not allow specific conclusions to be drawn, as hypotheses were impossible to be developed. New, more comprehensive works, involving other ICD implantation referral hospitals, are needed, especially given the highly prevalent Chagas disease in the Midwest Region of Brazil and the predominant cardiac manifestation of the disease in the population of Goiás state.
**Conclusion**

The clinical profile of patients with chronic Chagas disease with CDI was the following: male, aged 51-60, presence of dual-chamber devices, adequate use of antiarrhythmic drugs and beta-blockers, presence of systemic hypertension (SH), left ventricular ejection fraction (LVEF) between 35-45%, clinical admissions due to cardiac causes (particularly HF and ES), and zero and three post-implantation admissions.

**Potential Conflicts of Interest**

No relevant conflicts of interest.

**Sources of Funding**

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**Academic Association**

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