Relation of Interatrial Block to New-Onset Atrial Fibrillation in Patients with Chagas Cardiomyopathy and Implantable Cardioverter-Defibrillators

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Abstract. *Chagas cardiomyopathy (ChC) is an endemic disease in Latin America. A significant proportion of patients develop atrial fibrillation (AF), which may result in stroke and increased mortality. Interatrial block (IAB) has been associated with the development of AF in different clinical scenarios. The aim of our study was to determine whether IAB can predict new onset AF in patients with ChC and implantable cardioverter-defibrillators (ICDs). We conducted a retrospective study of patients with ChC and ICDs from 14 centers in Latin America. Surface ECGs were collected prior to device implantation. Partial IAB was defined as a P-wave > 120 ms and advanced IAB as a P-wave > 120 ms with biphasic morphology in inferior leads. AF events and ICD therapies were reviewed during follow-up. Eighty patients were analyzed. Mean age was 54.6±10.4 years, 52 (65%) male. Mean left ventricular ejection fraction was 40±12%. IAB was detected in 15 patients (18.8%), with 8 (10.0%) partial and 7 (8.8%) advanced. During a follow up of 33±20 months, 11 patients (13.8%) presented with new AF. IAB (partial + advanced) was strongly associated with new AF ($p<0.0001$) and inappropriate ICD therapies ($p=0.014$). In conclusion, IAB predicted new-onset AF in patients with ChC and ICDs.*

Keywords: Interatrial block, Chagas cardiomyopathy, Atrial fibrillation

1. Introduction

Chagas disease, caused by the parasite *Trypanosoma cruzi*, affects 8-10 million people in Latin America and almost 25% of them will develop chronic myocardial disease after years or decades (1). Up to one fifth of patients will develop atrial fibrillation (AF), which is associated with systemic thromboembolism and poor prognosis (2,3). Interatrial block (IAB), defined as a prolonged P-wave (> 120 ms) on a 12-lead electrocardiogram (ECG), has been associated with the development of AF in many clinical settings, probably through delayed and heterogeneous electrical activation of the left atrium (LA) (4). The aim of our study was to determine whether IAB can predict new onset AF in patients with ChC and implantable cardioverter-defibrillators (ICDs).

2. Methods

The present study was a retrospective analysis of patients with ChC and an ICD implanted for primary or secondary prevention at 14 Latin American centers.

The inclusion criteria were (i) ChC diagnosed by positive serologic tests and classic criteria including: living in endemic areas, ECG and chest X-ray criteria; (ii) ICD implanted for primary or secondary prevention of sudden cardiac death; (iii) Sinus rhythm. Patients with prior history of AF were excluded.

A standard 12-lead ECG was obtained in all patients prior to the device implantation. The P-wave duration was measured using semi-automatic calipers. Partial IAB (pIAB) was defined as a P-wave duration of > 120 ms without biphasic morphology (±) in the inferior leads, and

advanced IAB (aIAB) was defined as a P-wave > 120 ms and biphasic morphology (±) in the inferior leads (5). The ICD programming included therapy for ventricular tachycardia (VT) with antitachycardia pacing (ATP) followed by shock for ventricular fibrillation (VF).

The primary outcome was development of new onset AF. In single chamber devices AF was defined as an irregularly irregular rhythm lasting at least 30 seconds with > 80% match with the stored template. In devices with an atrial lead AF was defined as an episode of switch mode or atrial high rate lasting at least 30 seconds with electrograms compatible with fast and disorganized atrial rhythm. The secondary outcome was inappropriate ICD therapies, defined as ATP or shocks delivered by the ICD for any other rhythm rather than VT/VF. All patients attended regular follow-up visits, which were scheduled by the investigator at 3 to 6-month intervals.

Data were expressed as means and standard deviations for continuous variables and frequencies and percentages for categorical variables. Univariate comparisons and multivariate logistic regression analyses were performed to identify predictors of atrial fibrillation. P values < 0.05 were considered statistically significant.

3. Results

A total of 80 patients were analyzed. Baseline characteristics are summarized in Table 1. The indication for ICD was secondary prevention in 70%. Devices implanted were single chamber in 31%, dual chamber in 65% and resynchronization therapy in 4%.

Table 1. Baseline characteristics. LVEF = left ventricular ejection fraction; IAB = interatrial block; ARB = angotensin II receptor blockers; ACEI = angiotensin-converting-enzyme inhibitors.

Variable	Mean ± SD or %
Age (years ± SD)	54.6 ± 10.4
Male sex (%)	65
LVEF (% ± SD)	40 ± 12
Primary prevention (%)	30.0
Secondary prevention (%)	70.0
Functional capacity (%): I	45.0
II	38.8
III	16.2
P-wave duration (ms ± SD)	107.4 ± 12.6
IAB (%): Advanced	10.0
Partial	8.8
QRS duration (ms ± SD)	149.5 ± 80.5
Medical treatment (%)	
- Amiodarone	71.2%
- β-Blockers	60.0%
- ARB, ACEI	58.8%
- Spironolactone	35.0%

Mean P-wave duration was 107.4 ± 12.6 ms and IAB was detected in 15 patients (18.8%): 8 partial (10.0%; P-wave duration 126.2 ± 13.8 ms) and 7 advanced (8.8%; P-wave duration 129.7 ± 8.9 ms). Right bundle branch block (RBBB) was present in 42.5% of patients. Figure 1 shows a pattern of advanced IAB in a patient with typical ECG abnormalities of Chagas, which include RBBB and/or left anterior fascicular block (1).

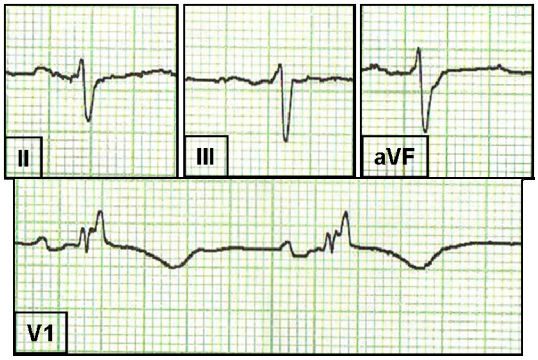

Fig. 1. Inferior + V1 leads of a patient with ChC and ICD.

During a follow up of 33 ± 20 months, 11 patients (13.8%) presented with new AF. The occurrence of AF in the group with IAB was 11/15 (73.3%) versus 0/65 (0%) in patients with normal P-wave duration ($p<0.0001$). Fourteen patients presented with inappropriate therapies during the follow-up (17.5%), all of them due to AF with rapid ventricular response. Seven patients died during the study period (8.8%).

Table 2. Comparison of patients with and without AF. AF = atrial fibrillation; LVEF = left ventricular ejection fraction; IAB = interatrial block.

Clinical variable	No AF (n = 69)	AF (n = 11)	p
Age (years ± SD)	53.7 ± 10.7	59.6 ± 6.8	0.08
Male sex (%)	63.8	72.7	0.56
LVEF (% ± SD)	40.9 ± 12.4	35.1 ± 9.2	0.14
P-wave duration (ms)	104.5 ± 10.8	125.3 ± 7.8	**< 0.0001**
IAB (%)	6.0	100.0	**< 0.0001**
QRS duration (ms ± SD)	128.8 ± 30.6	146.4 ± 23.8	0.07
Amiodarone (%)	69.6	81.8	0.40
Betablockers (%)	60.9	54.5	0.69

Table 2 shows a comparison of patients with and without AF. P-wave duration was significantly longer in patients that developed AF compared with those who did not (125.3 ± 7.8 vs 104.5 ± 10.8 ms; $p<0.0001$) and the prevalence of IAB was also significantly higher in the first group (100.0 vs 6.0%; $p<0.0001$).

In the univariate analysis IAB (partial + advanced) remained strongly associated with inappropriate therapies by the ICD (OR 4.8, 95% CI 1.3, 16.9, $p=0.014$). However, it was not possible to develop a multivariable model for AF because all 11 of the AF cases had IAB, resulting in an unstable model.

4. Discussion

The results of this study demonstrate that the presence of IAB in ChC is associated with the development of new onset AF. This is relevant considering that this arrhythmia is a major cause of stroke in this population (6) and an established predictor of poor prognosis.

The development of AF in ChC is mostly related to LA remodeling associated with progressive ventricular dysfunction. LA diameter annual variation rate, a marker of atrial remodeling, has been found to be related to the severity of heart involvement in ChC and it was associated with new onset AF (7). In addition, the inflammatory substrate of the disease may also play a pathogenic role. Parasite-dependent inflammation and immune mediated

cardiac injury result in destruction of cardiac myocites, regional fibrosis and potential substrate for reentry atrial arrhythmias.

The role of interatrial conduction disorders in the genesis of atrial arrhythmias was described long ago by Bayés de Luna et al. (8) and later confirmed by others. Intra and interatrial conduction delays lead to dispersion of refractory periods and participate in initiating and maintaining reentry circuits by promoting the occurrence of unidirectional block. Thus, a prolonged P-wave duration on 12-lead ECG or signal-averaged electrocardiography (SAECG) has been associated with new-onset AF (9), recurrence of AF after electrical or pharmacological cardioversion (10,11), AF recurrence after pulmonary vein isolation (12), and progression of paroxysmal AF to the persistent or permanent forms of the disease (13,14). Our findings are also in agreement with data reported for other cardiomyopathies such as hypertrophic or hypertensive cardiomyopathy and ischemic heart disease.

In conclusion, the presence of IAB (partial + advanced) predicted new onset AF in patients with ChC and ICDs, leading to increased risk of inappropriate therapies.

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