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Value of the Qrs-T Angle in Predicting the Induction of Ventricular Tachyarrhythmias in Patients with Chagas Disease

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Abstract

Background: The QRS-T angle correlates with prognosis in patients with heart failure and coronary artery disease, reflected by an increase in mortality proportional to an increase in the difference between the axes of the QRS complex and T wave in the frontal plane. The value of this correlation in patients with Chagas heart disease is currently unknown.

Objective: Determine the correlation of the QRS-T angle and the risk of induction of ventricular tachycardia / ventricular fibrillation (VT / VF) during electrophysiological study (EPS) in patients with Chagas disease.

Methods: Case-control study at a tertiary center. Patients without induction of VT / VF on EPS were used as controls. The QRS-T angle was categorized as normal (0–105º), borderline (105–135º) or abnormal (135–180º). Differences between groups for continuous variables were analyzed with the t test or Mann-Whitney test, and for categorical variables with Fisher's exact test. P values < 0.05 were considered significant.

Results: Of 116 patients undergoing EPS, 37.9% were excluded due to incomplete information / inactive records or due to the impossibility to correctly calculate the QRS-T angle (presence of left bundle branch block and atrial fibrillation). Of 72 patients included in the study, 31 induced VT / VF on EPS. Of these, the QRS-T angle was normal in 41.9%, borderline in 12.9% and abnormal in 45.2%. Among patients without induction of VT / VF on EPS, the QRS-T angle was normal in 63.4%, borderline in 14.6% and abnormal in 17.1% (p = 0.04). When compared with patients with normal QRS-T angle, those with abnormal angle had a fourfold higher risk of inducing ventricular tachycardia / ventricular fibrillation on EPS [odds ratio (OR) 4; confidence interval (CI) 1.298-12.325; p = 0.028]. After adjustment for other variables such as age, ejection fraction (EF) and QRS size, there was a trend for the abnormal QRS-T angle to identify patients with increased risk of inducing VT / VF during EPS (OR 3.95; CI 0.99-15.82; p = 0.052). The EF also emerged as a predictor of induction of VT / VF: for each point increase in EF, there was a 4% reduction in the rate of sustained ventricular arrhythmia on EPS.

Conclusions: Changes in the QRS-T angle and decreases in EF were associated with an increased risk of induction of VT / VF on EPS. (Arq Bras Cardiol. 2014; 103(6):460-467)

Keywords: Tachycardia, Ventricular; Arrhythmias, Cardiac; Chagas Disease; Electrocardiography; Case-Control Studies.

Introduction

Chagas disease is a prevalent public health problem in Brazil and Latin America. The disease has been gaining importance in developing countries due to intense migration of individuals from places historically considered to be reservoirs of the disease[1]. It is caused by the parasite *Trypanosoma cruzi* transmitted vectorially through the bite of triatomine insects, from mother to fetus, orally or through transfusion of contaminated blood[2].

The physiopathology of the disease involves inflammation, tissue destruction and fibrosis of cardiac cells leading to dysautonomia, microcirculatory changes and damage to the muscle heart and to the intramural nervous system[1]. The disease occurs in indeterminate, non-cardiac or cardiac forms. The cardiac form is further subdivided into with or without ventricular dysfunction. Even with normal ejection fraction, patients with Chagas heart disease may progress with several cardiac conduction disorders and severe ventricular arrhythmias which emerge as important prognostic predictors.

Tachyarrhythmias (ventricular tachycardia and ventricular fibrillation) and heart failure are the most common cardiovascular causes of mortality in patients with Chagas disease[1,3,4]. Tachyarrhythmias may be preceded by typical symptoms or even progress to sudden death without premonitory signs, which may also affect individuals with structurally normal hearts. Considering the prevalence of Chagas disease and the increase in life expectancy, risk stratification for sudden death and tachyarrhythmias is of extreme importance in public health.

The QRS-T angle is an electrocardiographic variable that determines the directions of depolarization and repolarization of the heart in the frontal plane. In normal conditions, these

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processes have the same spatial orientation but in opposite directions. Differences between both indicate electrical cardiac abnormalities that signal structural myocardial changes affecting depolarization or regional changes in repolarization sequence. Studies show that a simple tool - the electrocardiogram - offers information for risk stratification based on analysis of the QRS-T angle. However, no studies have evaluated the importance of this variable and its association with induction of malignant ventricular arrhythmias during programmed ventricular stimulation in patients with Chagas heart disease.

The aim of this study was to determine whether the QRS-T angle obtained in the frontal plane during a 12-lead resting electrocardiogram is associated with increased risk of induction of ventricular arrhythmia during electrophysiologic study (EPS) in patients with Chagas disease.

Methods

Study planning

This is a retrospective study that included patients with Chagas disease who underwent EPS at *Instituto Dante Pazzanese de Cardiologia* within the past three years. Patients were divided into two groups according to induction or not of malignant ventricular arrhythmias (sustained ventricular tachycardia, ventricular fibrillation or ventricular flutter) in response to the protocol of ventricular stimulation during the EPS. Collected information included demographic data (age, gender, history of systemic arterial hypertension, diabetes mellitus, dyslipidemia, coronary artery disease, stroke, syncope, use of concomitant medications), electrocardiographic data (rhythm, presence of atrioventricular and intraventricular block, QRS interval and QRS-T angle); echocardiographic data (ejection fraction, right ventricular dysfunction, presence of thrombi or aneurysms) and results of 24-hour Holter monitoring (quantification of ventricular extrasystoles, nonsustained and sustained ventricular tachycardias). These data were obtained from medical records, registered in forms specifically designed for the study and then correlated with EPS findings. Patients were not followed up and the data were collected from records, tests and chart notes.

Cohort of patients

The study included all patients with at least two positive serological tests for Chagas disease who underwent EPS over the previous three years. Information collected about the cohort included medical history and use of medications. Patients with blood pressure ≥ 140 / 90 mmHg[5] or using antihypertensive drugs were labeled hypertensive. Serum fasting glucose levels above 126 mg/dL on two occasions or use of oral hypoglycemic agents or insulin was determined as diabetes mellitus. The analysis excluded individuals with cardiomyopathy of other etiologies (coronary artery disease, hypertension, or others), atrial fibrillation, left bundle branch block and those with rhythm determined by a pacemaker. The diagnosis of coronary artery disease was determined by coronary angiography showing at least 70% of stenosis on the affected artery.

Definition of events

Sustained ventricular tachycardia was defined as the occurrence of tachycardia arising from the ventricle with a heart rate above 100 bpm and duration above 30 seconds or associated with clinical or hemodynamic instability. A rapid, disordered, and ineffective ventricular activity characterized the diagnosis of ventricular fibrillation.

Electrocardiogram

The QRS complex and T wave axes on the frontal plane were calculated based on an analysis of the (12-lead) resting electrocardiogram recorded at 25 mm / sec and with amplitude of 10 mm / mV. In both situations, the axis was located on the lead with highest QRS complex and T wave amplitudes. The difference between the angles of the QRS complex and T wave was calculated as the absolute difference between the angles, with values between 0º and 180º. These measurements were determined by two independent reviewers. In case of disagreement, a third reviewer was prompted. The QRS-T angle was categorized in three groups: normal (0–105º), borderline (105–135º) and abnormal (135–180º).

Holter monitoring

24-hour Holter monitoring offered information about the occurrence of ventricular extrasystole and ventricular tachycardia. Ventricular extrasystole was defined as the occurrence of an isolated or coupled beat arising in the ventricle. The occurrence of at least three consecutive ventricular beats with a rate above 100 bpm was defined as nonsustained ventricular tachycardia and, when lasting more than 30 seconds, as sustained ventricular tachycardia.

EPS

All patients underwent EPS according to the standard routine protocol adopted at the institution. The protocol consists of programmed ventricular stimulation with two basic cycles (600 and 500 ms), with up to three extrastimuli at the apex and outflow tract of the right ventricle, in addition to rapid stimulation (up to 250 ms) of the same sites. The first extrastimulus, coupled with the last QRS of the burst pacing and 50 ms faster than the ventricular refractory period, is applied during late diastole. The coupling interval is shortened every 10 ms until the refractory period is reached. The second and third extrastimuli, which are similar to the first, are then introduced in sequence. In the event of ventricular tachycardia, cardioversion to sinus rhythm was performed with rapid ventricular stimulation or, in case of hemodynamic collapse, electrical cardioversion.

Echocardiogram

Echocardiographic assessments included measurement of left atrial diameter, left ventricular systolic and diastolic diameters, left ventricular ejection fraction and, when present, determination of diastolic dysfunction, right ventricular dysfunction, and left ventricular thrombus or aneurysm.

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Statistical Analysis

Continuous variables were described as mean and standard deviation, and as interquartile range when appropriate. Categorical variables were presented as relative and absolute frequencies. Differences between groups regarding the induction or not of ventricular arrhythmias were analyzed with the t test or Mann-Whitney test for continuous variables, and with Fisher's exact test for categorical variables. Logistic regression models were applied to identify potential factors influencing the groups in combination. Backward stepwise regression was applied to select the variables, with an alpha-to-remove of 5%. P values below 0.05 were considered statistically significant. Retrieved data were analyzed with the softwares Microsoft Excel and R for Windows.

Results

Between January and July 2013, a total of 116 charts of patients with Chagas disease who underwent EPS were selected. Of these, 44 (37.9%) were excluded due to the following reasons: 18 (15.5%) for incomplete data, 6 (5.2%) for inactive records and 19 (16.4%) in which the calculation of the QRS-T angle was impractical. Of the reasons that precluded the calculation of the QRS-T angle were the occurrence of left bundle branch block in 16 (13.8%) and atrial fibrillation in 3 (2.6%). The final analysis, therefore, included 72 patients.

Mean age was 59.3 ± 10.6 years and 35 patients (48.6%) were males. Mean ejection fraction was $49.8 \pm 16.1\%$ and more than half of the cohort had functional class I. Right bundle branch block and left anterior superior divisional block were observed in 41 (56.9%) and 47 (65.3%) patients, respectively. Almost 80% of the patients used angiotensin-converting enzyme inhibitors / angiotensin II receptor blockers, 54.2% used amiodarone and 47.2% used beta-blockers. The QRS-T angle was normal in 39 patients (54.2%), abnormal in 21 (29.2%) and borderline in 10 (13.9%).

Clinical, electrocardiographic, echocardiographic and Holter findings of the 72 patients included in the analysis are described in Table 1.

There were no differences in baseline characteristics between groups, except for age. These findings are shown in Table 2.

Statins and aspirin were the most commonly prescribed medications in the group without induction of malignant ventricular arrhythmias. Even though beta-blockers and spironolactone were used more often in the group with induction of arrhythmias, this difference did not reach statistical significance (Table 3).

A QRS complex duration greater than 120 ms was observed more frequently in patients without induction of sustained ventricular arrhythmias. Among patients with induction of ventricular arrhythmias on EPS, the QRS-T angle was normal in 13 (41.9%), borderline in 4 (12.9%) and abnormal in 14 (45.2%). In the group of patients without induction of ventricular arrhythmias, the QRS-T angle was normal in 26 (63.4%), borderline in 6 (14.6%) and abnormal in 7 (17.1%, p = 0.04). The frequency of ventricular extrasystoles on 24-hour Holter was higher in individuals without induction of

ventricular arrhythmias on EPS (70.3% versus 60.7%), however, this finding showed no statistical significance (p = 0.71).

Mean left ventricular ejection fraction in the group with induction of ventricular arrhythmia was 42.6%, compared with 55.1% in the group without induction of ventricular arrhythmias (p = 003, Tables 4 and 5).

Figure 1 shows findings from a patient with abnormal QRS-T angle who induced sustained ventricular tachycardia on EPS.

On logistic regression analysis, ejection fraction emerged as a strong predictor of induction of ventricular tachycardia / ventricular fibrillation in this cohort. For each point increase in the ejection fraction there was a reduction of approximately 4% on the induction rate of ventricular tachycardia / ventricular fibrillation on EPS. Compared with patients with normal QRS-T angle, those with abnormal angle had a fourfold increased risk of inducing ventricular tachycardia / ventricular fibrillation during EPS [odds ratio (OR) 4; confidence interval (CI) 1.298-12.325; p=0.028]. After adjustment for other variables such as age, ejection fraction and QRS size, there was a trend in the abnormal QRS-T angle to identify patients with increased risk of induction of VT / VF during EPS (OR 3.95; CI 0.99-15.82; p = 0.052, Table 6).

Discussion

The results of this study show that patients with Chagas heart disease with abnormal QRS-T angle in the frontal plane tend to have a higher risk of inducing ventricular tachycardia / ventricular fibrillation during programmed ventricular stimulation on the EPS. This finding shows that an electrocardiographic variable may help clinicians establish a prognosis for future arrhythmic events in this population.

Abnormalities in ventricular repolarization are associated with increased susceptibility to complex arrhythmias[6]. Rassi et al[7] demonstrated that an abnormal ECG associated with symptoms of heart failure - functional class III or IV - determine a high mortality risk in patients with Chagas disease. This finding allows guidance of specific therapies directed to this subgroup of patients. In addition to that, the analysis of the amplitude and duration, as well as the spatial and frontal axes of the QRS-T angle have also been described in several clinical studies as strong and independent predictors of mortality in elderly patients[8,9], HIV patients receiving antiretroviral drugs[10], patients with coronary artery disease[11] and conditions such as acute coronary syndrome[12], post-acute myocardial infarction[13], heart failure[14] and nonischemic cardiomyopathy[15].

Previous studies have highlighted the importance of the QRS-T angle as an independent predictor of mortality in patients with Chagas disease[16-18]. However, until now, there had been no reports of the association between the value of the QRS-T angle on the induction of malignant arrhythmias in this population, which would reflect an increased possibility of high risk arrhythmic events in this population. In this study, the direct comparison between abnormal and normal QRS-T angles showed that the first was associated with a fourfold increased risk of induction of ventricular arrhythmia during EPS, highlighting the importance of this simple electrocardiographic variable in risk stratification of a population with such severe cardiopathy.

Table 1 - Clinical, electrocardiographic, echocardiographic and Holter findings of 72 patients with Chagas disease

Characteristics	N (%)
Clinical characteristics	
Age in years (mean ± standard deviation)	59.3 ± 10.6
Male gender	35 (48.6)
Dyslipidemia	27 (37.5)
Syncope	43 (59.7)
Smoking	5 (6.9)
Stroke or TIA	7 (9.7)
Systemic arterial hypertension	55 (76.4)
Diabetes mellitus	10 (13.9)
Implantable cardioverter	2 (2.8)
Pacemaker	2 (2.8)
Functional class	
I	37 (51.4)
II	30 (41.7)
III	5 (6.9)
IV	0 (0.0)
Concomitant medications	
Beta-blockers	34 (47.2)
Amiodarone	39 (54.2)
ACE inhibitors/ABRs	57 (79.2)
Furosemide	18 (25.0)
Statins	21 (29.2)
Aspirin	30 (41.7)
Oral anticoagulant	2 (2.8)
Spironolactone	19 (26.4)
Electrocardiographic features	
First degree ABV	22 (30.6)
Right bundle branch block	41 (56.9)
Left anterior superior hemiblock	47 (65.3)
QRS < 120 ms	24 (33.3)
QRS > 120 ms	48 (66.7)
Normal QRS-T angle	39 (54.2)
Abnormal QRS-T angle	21 (29.2)
Borderline QRS-T angle	10 (13.9)
Echocardiographic characteristics	
Ejection fraction (mean)	49.8 ± 16.1%
Diastolic dysfunction	42 (58.3)
Systolic dysfunction	3 (4.2)
Intracardiac thrombus	1 (1.4)
Left ventricular aneurysm	3 (4.2)
Holter findings	
0–10 ventricular extrasystoles / hour	12 (16.7)
11–30 ventricular extrasystoles / hour	10 (13.9)
> 31 ventricular extrasystoles / hour	43 (59.7)
Nonsustained ventricular tachycardia	37 (51.4)

TIA: transitory ischemic attack; ACE: angiotensin-converting enzyme; ABRs: angiotensin II receptor blockers; ABV: atrioventricular block.

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Table 2 - Comparison of clinical characteristics between groups

Clinical characteristics	Ventricular tachycardia / ventricular fibrillation induction		
	No 41 (56.4%)	Yes 31 (43.1%)	p value
Age (years)	61.98	55.77	0.01
Male gender	16 (39)	19 (61.3)	0.09
Dyslipidemia	16 (39)	11 (35.5)	0.81
Syncope	24 (58.5)	19 (61.3)	1.00
Smoking	3 (7.3)	2 (6.5)	1.00
Previous stroke / TIA	5 (12.2)	2 (6.5)	0.69
Systemic arterial hypertension	30 (73.2)	25 (80.6)	0.58
Diabetes mellitus	6 (14.6)	4 (12.9)	1.00

TIA: transitory ischemic attack.

Table 3 - Comparison between groups regarding use of concomitant medications

Concomitant medications	Induction of ventricular tachycardia / ventricular fibrillation		
	No 41 (56.4%)	Yes 31 (43.1%)	p value
Beta-blocker	15 (36.6)	19 (61.3)	0.06
Amiodarone	22 (53.7)	17 (54.8)	1.00
ACE inhibitors/ABRs	33 (80.5)	24 (77.4)	0.78
Furosemide	10 (24.4)	8 (25.8)	1.00
Statins	16 (39.0)	5 (16.1)	0.04
Aspirin	22 (53.7)	8 (25.8)	0.03
OA	2 (4.9)	0 (0.0)	0.50
Spironolactone	8 (19.5)	11 (35.5)	0.18

ACE: angiotensin-converting enzyme; ABRs: angiotensin II receptor blockers; OA: oral anticoagulant.

Table 4 - Comparison of electrocardiographic findings between groups

Electrocardiographic findings	Induction of ventricular tachycardia / ventricular fibrillation		
	No 41 (56.4%)	Yes 31 (43.1%)	p value
First degree AVB	12 (29.3)	10 (32.3)	0.80
Right bundle branch block	25 (61.0)	16 (51.6)	0.48
Left anterior superior hemiblock	29 (70.7)	18 (58.1)	0.32
QRS < 120 ms	16 (39.0)	8 (25.8)	0.016
QRS < 120 ms	25 (61.0)	23 (74.2)	0.88
QRS-T angle			
Normal	26 (63.4)	13 (41.9)	
Borderline	6 (14.6)	4 (12.9)	0.04
Abnormal	7 (17.1)	14 (45.2)	

ABV: atrioventricular block.

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Table 5 - Comparison of echocardiographic and Holter findings between groups

Findings of echocardiogram and Holter	Induction of ventricular tachycardia / ventricular fibrillation		
	No 41 (56.4%)	Yes 31 (43.1%)	p value
Left ventricular diastolic dysfunction	26 (63.4)	16 (51.6)	0.47
Right ventricular dysfunction	1 (2.4)	2 (6.5)	0.57
Left ventricular thrombus	0 (0.0)	1 (3.2)	0.42
Left ventricular aneurysm	3 (7.3)	0 (0.0)	0.26
Mean ejection fraction	55.12	42.57	0.03
0–10 ventricular extrasystoles / hour	6 (14.6)	6 (19.4)	
11–30 ventricular extrasystoles / hour	5 (12.2)	5 (16.1)	0.71
> 31 ventricular extrasystoles / hour	26 (63.4)	17 (54.8)	

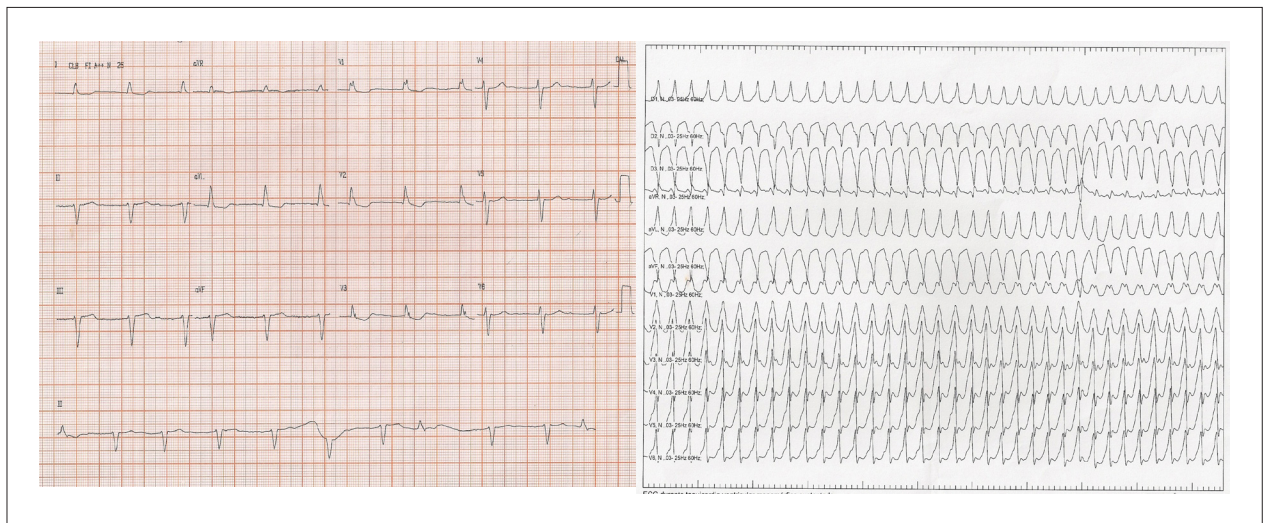
Figure 1 - Left, electrocardiogram showing abnormal QRS-T angle (SÂQRS= -70º; SÂT = +100º; QRS-T 170º angle). Right, sustained monomorphic ventricular tachycardia induced during electrophysiological study of the same patient.

The ideal method of calculating the QRS-T angle is a matter of discussion. The angle may be determined by spatial calculation or by a simple difference between the angles of the QRS complex and the T wave in the frontal plane. However, the spatial calculation requires the Frank leads (X, Y, Z), which are not always available in conventional electrocardiographs, making this calculation less practical. In contrast, the determination of the difference between the angles in the frontal plane (the technique adopted in this study) is more practical, and of easy reach and interpretation in clinical practice. Zhang et al. demonstrated that the determination of the QRS-T angle in the frontal plane shows good correlation with the findings obtained on spatial determination[11]. However, Brown and Schlegel[19], when comparing the mean spatial QRS-T angle with frontal plane QRS-T angles determined by conventional electrocardiogram and vectorcardiogram of 370 patients with cardiac disease confirmed by imaging tests (coronary artery disease, hypertrophic cardiomyopathy, or ventricular systolic dysfunction) and 210 apparently normal individuals, identified a statistically significant difference favoring a stronger prognostic power for the spatial method. The authors interpreted this result as decisive to suggest that the frontal plane QRS-T angle should not be used to replace the spatial QRS-T angle. In contrast, a recent study by Aro et al[20] assessing the QRS-T angle in the frontal plane demonstrated that 2% of a population of 10,957 individuals had a difference > 100 degrees and a higher rate of sudden death from arrhythmic causes and total mortality when compared with those with normal QRS-T angle. These along with Zhang's data support the adoption of the simple difference between the axes of the QRS complex and T wave in the frontal plane as equally useful in determining the risk of induction of ventricular tachycardia / ventricular fibrillation in patients with Chagas disease undergoing EPS.

The presence of fibrotic areas or tissues with low capacity to conduct electricity may modify the process

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Table 6 - Multivariate analysis in patients who induced ventricular tachyarrhythmia during EPS

	Induction of ventricular tachycardia / ventricular fibrillation Ventricular		
	OR	p value	CI
Age > 65 years	0.25	0.04	0.06 – 0.97
Ejection fraction < 35%	4.84	0.02	1.23 – 19.09
Beta-blocker use	1.30	0.64	0.39 – 4.33
QRS < 120 ms	1.35	0.65	0.37 – 4.90
QRS-T angle			
Normal			
Borderline	1.23	0 80	0.24 – 6.14
Abnormal	3.95	0.052	0.99 – 15.82

of cardiac depolarization and repolarization, representing therefore an area with a reentrant circuit. Abnormalities in activation and recovery of electrical activity, obtained by differences between the angles of the QRS complex and the T wave in the frontal plane may suggest the presence of this circuit and were, therefore, probably associated with a an increased probability of induction of ventricular tachycardia in this population of patients with Chagas disease.

Lastly, it should be emphasized that a left ventricular systolic dysfunction was associated with increased induction of malignant ventricular arrhythmias in the studied population. These results corroborate evidence published recently by our group and reflect the prognostic value of arrhythmogenic circuits secondary to fibrotic areas intermixed with normal conduction tissue[21].

Limitations

The limitations of this study include its observational retrospective nature, the small sample size and the collection of data from charts. The protocol of ventricular stimulation was similar for all patients, since it follows a methodology proposed by the group which has been routinely adopted for several years.

Conclusions

Changes in the QRS-T angle and ventricular dysfunction were associated with induction of severe ventricular

arrhythmias - ventricular tachycardia and fibrillation - during EPS in the cohort. The presence of ventricular extrasystoles or nonsustained ventricular tachycardia during 24-hour Holter monitoring, as well as clinical factors such as male gender and history of syncope, did not emerge as predictive factors for induction of such outcome.

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