Inducibility of ventricular arrhythmias in Chronic Chagas disease predicted by clinical scores.

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ABSTRACT

BACKGROUND

Clinical Scores can grade patients with Chronic Chagas disease according to their relative risk of death. Electrophysiologic Study (EPS) is a diagnostic tool that can further evaluate patients prone to arrhythmic death. **OBJECTIVE** To shed light on the causes of death in Chagas disease, specially on regards of importance of the VT induction and chances of death, as evaluated by Rassi clinical score. **METHODS** We evaluated data from 153 patients with Chagas disease from the electrophysiology laboratory from a tertiary center between January of 2011 and January 2013. All patients were evaluated with 1, 2, 3 or 4 ventricular extra-stimuli followed by runs of 10 beats fast ventricular stimulation. If VT or VF is inducible the patients are referred to ICD implant or VT ablation. **RESULTS** Of a total of 153 patients, 48% were male, mean age 58 ±12 years (24 - 84 years). As for associated diseases, 62% had high arterial blood pressure, 11% diabetes, 35% high cholesterol. There was no significant difference between the three groups regarding associated diseases.

As for risk of death according to the clinical score, 32% were evaluated as low risk, 35,4% intermediate, 32,6% high risk. NSVT on 24 hour Holter (p=0,009), stimulation on EPS (p<0,001), lower VEFE (p<0,01), cardiomegaly (p<0,001) and high risk on Rassi score (p<0,001) where the more associated variables to ventricular tachyarrithmias. **CONCLUSIONS** Clinical score is an interesting tool to further stratify patients in higher risk for VT induction during EPS, which is also a marker of higher risk of sudden cardiac death. Some characteristics as Non sustained VT, Pulmonary congestion, cardiomegaly

and low voltage QRS were the most relevant determinants for inducible VT on EPS. The duration of NSVT is also important for VT induction in EPS.

LIST OF Abbreviations:

chronic Chagas Cardiomiopathy = CCC, electrophysiologic Study = EPS, implantable cardioverter defibrillator = ICD, ventricular tachycardia = VT, ventricular fibrillation = VF, right ventricule = RV, left venctricule ejection fraction = LVEF, non-sustained VT = NSVT, electrocardiogram = ECG, high arterial blood pressure = HBP, diabetes = DB

Introduction

Chronic Chagas Disease is an infectious disease caused by a protozoa Trypanossoma Cruzy. Patients are usually infected by vetorial transmission (by contact with infected insects feces) and rarely by blood transfusion and congenital transmission. Chronic Chagas Cardiomiopathy (CCC) affects approximately 18 million patients and new cases accounts for nearly 200.000 each year[1]. Clinical Scores can grade patients according to their relative risk of death[2,3,4]. Electrophysiologic Study (EPS) is a diagnostic tool that can further evaluate patients prone to arrhythmic death, who can further benefit from a prophylactic implantable cardioverter defibrillator (ICD) implant[3]. Although widely used in patients with CCC, its relevance to clinical practice was evaluated in a limited number of patients and the relevance of ventricular tachycardia (VT) or ventricular fibrillation (VF) induction, as well as stimulation protocols were not adequately validated. This, to our knowledge, is the first study that can shed light on the causes of death in Chagas disease, specially on regards of importance of the VT induction and chances of death, as evaluated by Rassi clinical score.

METHODS

We evaluated data from 153 patients from a database of patients with Chagas disease from the electrophysiology laboratory from a tertiary center between January of 2011 and January 2013. All patients had at least two positive sorologic assays for chagas disease. All patients were evaluated with 1, 2, 3 or 4 ventricular extra-stimulation

followed by runs of 10 fast ventricular stimulation, first on the right ventricule (RV) apex and then on the RV outflow tract. The EPS was performed under mild sedation or local anaesthesia with lidocaine 2%.

As defined by the institutions protocol, all patients with the diagnosis of CCC are clinically evaluated by ECG, 24 hour Holter recordings and Transthoracic Echocardiography. Patients who present complex ventricular arrhythmias (non sustained VT, frequent ventricular ectopic beats) will be prescribed amiodarone 300-400mg/day for one month, and reevaluated afterwards. If the complex ventricular arrhythmias were not suppressed by then, or if the patient presents with syncope, sustained palpitations, dizziness at any point of the investigation, he is referred to EPS. If VT or VF is inducible the patients are referred to ICD implant. VT ablation is considered in stable, monomorphic VT with left venctricule ejection fraction (LVEF) higher than 40% and no history of syncope.

STATISTICAL ANALYSIS

Categorical variables are presented as full numbers and percentages. Continuous variables are presented as means and SD. The significance of baseline differences was determined by the chi-square test, Fisher's exact test, or the unpaired t-test, as appropriate. A two-sided P value of less than 0.05 was significant.

Patients were evaluated using clinical score (Rassi et al), and labeled as low risk, intermediate risk or high risk for death. They were also evaluated as VT inducible or non inducible by EPS protocol, and the risk of VT induction was designated for each group.

After the comparison of risk groups as regarding induction of VT, each characteristic that comprised the Rassi score was reevaluated individually through multivariate analysis.

RESULTS

Patients Characteristics

Of a total of 153 patients, 48% were male, mean age 58 ±12 years (24 - 84 years). As for associated diseases, 62% had high arterial blood pressure (HBP), 11% diabetes (DB), 35% high cholesterol. There was no significant difference between the three groups regarding associated diseases.

As for risk of death according to the clinical score, 32% were evaluated as low risk, 35,4% intermediate, 32,6% high risk. (see Figure 1)

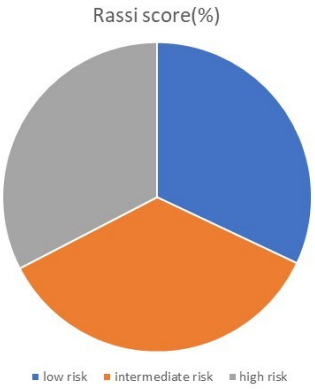

Figure 1: Participation of patients according to group risk allocation

Each component of the Rassi score was then evaluated in a multivariate analysis for the importance of each component. The patients were separated in two groups according to the outcome of the EPS(VT inducible or not). The prevalece of each characteristic was described in table 1 (also the difference between the groups highlighted on the right column)

	VT Inducible	VT not inducible	P
Age	56,7 ±11	59,7	0,129
Male sex	54%	42%	0,185
HBP	69%	57%	0,169
DM	7,3%	14,9%	0,288
High LDL	35,3%	35%	0,999
Current smoker	16,2%	10,4%	0,333
High BMI	5,8%	5,2%	0,999
Family History	4,4%	2,6%	0,666
Pulmonary congestion	24,2%	16,9%	0,303
LVEF	40 % ± 15	52%	<0,01
LVEDD	62,2 mm ±8	53,6 mm	0,03
LVEDS	46,4 mm ±17	39 mm	<0,01
NSTV Holter	75%	53.2%	0,009
Rassi Score Low	19,4%	41,2%	0,007
Rassi Score Intermediate	32,8%	35%	0,862
Rassi Score High	46%	12,5%	<0,001

Table 1: Patient characteristics and VT induction on EPS, HBP: High blood pressure, DM: Diabetes, NSVT: Non sustained VT, LVEF: Left ventricular Ejection fraction

Presence of Non sustained VT, Pulmonary congestion, cardiomegaly and low voltage QRS were relevant for inducible VT on EPS.

The characteristics of the non-sustained VT (NSVT) and VT induction were further compared, as for duration and higher ventricular rate. While longer NSVT on the last 24 hour Holter recording obtained from the patient prior to the EPS were related to higher VT induction, the ventricular rate of the NSVT was not relevant to the goal of the study. (See table 2)

	VT Inducible	**VT Non Inducible**	**p**
Maximum Rate (bpm)	142	146 bpm	0,955
Duration NSTV (number of QRS complexes)	12,3	6,1	0,014

Table 2: NSVT - Non sustained ventricular tachycardia(as evaluated by ambulatory EKG recording prior to EPS); VT- Ventricular tachycardia

DISCUSSION

Chagas disease has many presentations. Most patients with cardiac disease present with mild electrocardiogram (ECG) features, while the patients with structural disease and complex ventricular arrhythmias present the worst prognosis[5,6]. Death can come from bradyarrhythmias, tachyarrythmias, congestive heart failure or embolic events[7,8] . Most cardiologists struggle to find the importance of primary prevention by means of ICD placement. Others advocate that if we do not adequately select the patients prone to death by VT or ventricular fibrillation more accurately, the ICD placement supported by clinical scores or presence of complex arrhythmias can lead to worse prognosis and faster progression to heart failure.

The importance of the linear relation between the Rassi Score and VT induction on EPS leads to the understanding that these patients are more prone to ventricular tachyarrithmias and death as the score increases. That said, perhaps there is room for primary prevention on highest risk patients based on the clinical score refined by observation of the higher importance of some characteristics. In our study, those were NSVT on 24 hour Holter (p=0,009), stimulation on EPS (p<0,001), lower VEFE (p<0,01), cardiomegaly (p<0,001) and high risk on Rassi score (p<0,001).

Development of a clinical score by *Rassi et al* was a cornerstone in the way we evaluate the prognosis of patients with chagas disease. With the development of a clinical, bedside score, with easily obtained characteristics, they fed the clinician with data so that they could weight adequately their findings and reach a wiser management of cases. Some questions were left unanswered and we believed we could shed some light. The characteristics of NSVT were not evaluated. Although

intuitively the fastest NSVT were scarier, it was not relevant to VT induction in our patients. Duration though, were associated with a higher VT induction if the patient presented with longer NSVT. Unfortunately we were not able to develop a reliable cut-off for the duration of the NSVT.

Induction of VT during EPS is a marker for worst prognosis in several studies, specifically during amiodarone use. It could not be used as a firm surrogate for death, though, even in a disease not fully comprehended. As described before, death in CCC can be due to many different causes not related to VT.

Another limitation of the study was the selection of patients. As a tertiary center, we receive higher risk patients from the entire country. Our patients might not represent the lowest risk patients, the ones found on daily basis on cardiology clinics. Even so, there was a uniform distribution of low, intermediate and high risk patients in our population.

Still, this is one of the largest cohorts of CCC patients referred to EPS in a tertiary center nowadays. The patient characteristics adequately represent the patients currently under care of electrophysiology specialists.

CONCLUSION

Chagas disease can lead to death by many different ways. Clinical scores can identify the patients in higher risk of death by many causes. Clinical score is also an interesting tool to further stratify patients in higher risk for VT induction during EPS, which is also

a marker of higher risk of sudden cardiac death. Some characteristics as Non sustained VT, Pulmonary congestion, cardiomegaly and low voltage QRS were the most relevant determinants for inducible VT on EPS. The duration of NSVT might also be of relevance for VT induction in EPS.

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