

Study protocol

Proposal Title: QRS complex in Chagas patients in the early stage of Chagas heart disease. Relation to MRI findings.

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Keywords

Electrocardiogram, cardiac MRI (cMRI), QRS complex, left ventricular mass (LVM).

Background and rationale

Chagas disease is a serious public health problem in Latin America and an emerging problem in non-endemic countries, because of early mortality and substantial disability caused by this disease. Dilated cardiomyopathy, characterized by heart failure, ventricular arrhythmias leading to sudden death are the most important and severe manifestations of human chronic Chagas disease. Dilated cardiomyopathy is mostly a late manifestation of Chagas heart disease, and is characterized as a chronic myocarditis that involves all cardiac chambers and conduction system.

The occurrence and severity of cardiac damage depend on the stage of the disease. In a severe acute phase < 1% of patients develop acute myocarditis, pericardial effusion. In the chronic phase without demonstrable pathology (normal clinical findings, ECG and conventional chest radiography), there is a presence of infection (positive serological tests). About one third of patients evolve a chronic form with demonstrable pathology with a progressive damage of myocardium. Patients in the early stage present no symptoms of heart failure and no structural heart disease, including a normal ECG, Rx and echo. Patients in the following stages are still asymptomatic, however ECG changes (arrhythmias or conduction disorders) already occur. The more advanced stages represent gradually more advanced cardiac pathology, with maximum in the later stages with the presence of heart failure at rest.

It follows that the ECG's differences between early and later stages are basically findings of arrhythmias or conduction disorders. However, both of them represent already a serious impairment of the electrical properties of working myocardium and of conducting system. Therefore, in this study we will focus on the early stage of the Chagas disease, to identify early signs of impairment of the electrical properties of myocardium, before a well recognized "classical" ECG patterns develop.

It is obvious that both active and passive electrical properties in Chagas disease are altered, and vary/ evolve during the progression of Chagas disease. We have shown in our previous model simulation studies that impaired electrical properties of myocardium are reflected in QRS

complex changes, though some of these changes do not exceed normal limits according to traditional ECG criteria. We have also shown that impaired electrical properties (reduction in intercellular coupling, slowed conduction velocity) in the left ventricle resulted in the whole spectrum of QRS patterns, that did not depend on the anatomical shape of the ventricle. We have concluded that electrical remodeling could be the unified hypothesis for the broad spectrum of QRS patterns.

Traditionally, discrepancies between anatomical/ structural changes of the heart and ECG findings are perceived as a limitation of electrocardiography. We hypothesize that: (1) discrepancies between ECG and cMRI findings could provide additional information on the electrical remodeling of the myocardium in Chagas patients, and (2) subtle QRS complex changes, as analogous to those demonstrated with impaired conduction in the simulation studies, could be present in Chagas patients before arrhythmias and conduction disturbance occur.

In this study we will focus on the chronic phase without demonstrable pathology of the disease. We will be interested in ECG changes depending on the stage of the disease and in relation to MRI findings.

Material and Methods

Study population:

Positive chronic phase Chagas patients (the expected number of patients tbc: Laura).

Inclusion criteria:

Positive serological tests (please, define)

Good quality ECG and cMRI

ECG within normal limits

Clinical findings within normal limits???

Exclusion criteria:

Demonstrable pathology (clinical, biochemical, ECG, chest x-Ray, echo???? – please complete)

Design of the study: prospective, cross-sectional study

Methods:

12-lead electrocardiogram

Cardiac MRI

Variables: see the Table

References

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Participant characteristics/ variables:

	Chagas patients without demonstrable pathology	Comments
Age		
Sex		
Weight		
Height		
Body mass index		
Systolic blood pressure		
Diastolic blood pressure		
Total cholesterol		
HDL-cholesterol		
Chest X-ray		
Echocardiography???		
Serological tests		
Therapy		
ECG		
QRS duration		
QRS axis		
Amplitude of Q, R, S, R' waves in all leads of the 12-lead ECG		
QRSmax*		
QRSmax/LVM ratio		
ST segment deviation in all leads of 12-lead ECG		
leads with fQRS		
cMRI		
LV mass		

End-diastolic volume		
End-systolic volume		
LV ejection		
Location of the areas of hyperenhancement		
Volume of the hyperenhancement (per cent of total myocardium? or of the left ventricle?)		

***The maximum spatial vector magnitude (QRSmax):**

$$QRS_{max} = \sqrt{V2^2 + aVF^2 + V5^2}$$

Where V2 is the maximum QRS deflection in lead V2, aVF is the maximum QRS deflection in lead aVF and V5 is the maximum QRS deflection in lead V5.