Evaluation of Myocardial Damage in Chagasic Patients from the Signal-Averaged and Beat-to Beat Analysis of the High Resolution Electrocardiogram

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Abstract

The aim of this work was to compare the results of the signal-averaged and beat-to-beat analysis of the high resolution electrocardiogram (HRECG) of 96 chronic chagasic patients classified in different groups (I, II and III) according to their degree of myocardial damage. For comparison, the HRECGs of 11 healthy subjects used as control group (Group O) were also examined. In the signal-averaged analysis, three standard indexes were computed from the vector magnitude of the filtered and averaged XYZ leads: a) the QRS duration (QRSD); b) the RMS voltage of the terminal 40 ms (RMS40) and c) the duration of the terminal low amplitude signal below 40 μV (LAS40). In the beat-to-beat analysis, the variability of the QRS duration (ΔQRSD) was calculated. It has been found that two or more indexes exhibited statistical differences ($p<0.05$) between groups 0-II, O-III, I-II, I-III and II-III. We concluded that the signal-averaged and beat-to-beat analysis of HRECG is a promising diagnosis technique to evaluate the degree of myocardial damage in chronic chagasic patients.

1. Introduction

Chagas' disease is a tropical illness caused by a parasite, *Trypanosoma Cruzi*, which is transmitted by a blood-sucking triatomine bug. This illness is the major cause of cardiac disease in South and Central America. It is estimated that 16 to 18 million Latin Americans have been infected and that 2-3 million may have already developed chronic complications [1].

There are two stages of the disease: the acute stage which appears shortly after the infection, and the chronic stage which appears after a silent and asymptomatic period that may last 10-20 years [2]. The chronic phase is characterized by a progressive inflammation of cardiac muscle (Chagasic myocarditis) that produces a destruction of cardiac fibers and a fibrosis in multiple areas of the myocardium [3]. This cardiac damage usually has slow, progressive and irreversible characteristics and the symptoms appear when the damage is significant. In order to establish the correct treatment in chronic chagasic patients, it is necessary to determine previously the degree of myocardial damage produced by the disease. Currently, this clinical evaluation is made by different diagnostic procedures, such as X-ray, echocardiogram, conventional electrocardiogram (ECG), and ambulatory ECG (Holter).

In the last decade, the use of the high-resolution ECG (HRECG) has been proposed to determine the degree of cardiac damage in chronic chagasic patients [4]. This electrocardiographic technique is oriented specifically to the detection of cardiac micropotentials, such as ventricular late potentials (VLP). The VLP are low-level, high frequency, fractionated signals within the terminal region of the QRS complex and the beginning of the ST segment. Due to their low amplitude, VLP are usually masked by the background noise in HRECG records.

Classically, the most commonly used method to improve the signal to noise ratio of VLP is the coherent signal averaging, which assumes that micropotentials of interest are reproducible and that the noise is white. Using signal-averaging methods, different studies have detected the presence of VLP in HRECG records of chronic chagasic patients [5,6]. However, the process of averaging eliminates any dynamic information of VLP that could be of diagnostic utility. In previous work [7], we showed that chronic chagasic patients with severe myocardial damage have a higher beat-to-beat variability of the QRS duration compared with healthy subjects, reflecting the possible presence of variable VLP.

In this work, we propose the application of signal-averaged and beat-to-beat temporal analysis of HRECG of chronic chagasic patients, in order to determine the most significant indexes that for evaluating the degree of myocardial damage produced by the disease.

2. Materials

In this work, we analyzed the HRECG of 96 chronic chagasic patients and 11 healthy subjects. All HRECG were recorded during 10 minutes according to the accepted standard [8], using orthogonal XYZ leads. The sampling rate was 1000 Hz and the A/D resolution was 16 bits. All data were extracted from Chagas Database [9] of the Simon Bolivar University, Venezuela.

Subjects were clinically classified into 4 groups, as follow:

- *Group O* composed of 11 healthy subjects, blood sero-negative.
- *Group I* consisted of 41 chagasic patients, blood sero-positive, but no echocardiographic or standard ECG evidence of myocardial damage.
- *Group II* included 39 chagasic patients, blood sero-positive, with some evidence of cardiac involvement detected in 24 hours Holter monitoring.
- *Group III* included 16 chagasic patients, blood sero-positive, with evidences of severe myocardial damage observed in conventional ECG and documented episodes of ventricular tachycardia.

3. Methods

3.1. Signal-averaged temporal analysis

Temporal analysis is the standard technique for the detection of VLP in signal-averaged HRECG records [8]. This technique is based on the evaluation of 3 temporal indexes computed from the vector magnitude (VM) of the filtered and averaged signals of XYZ leads.

Figure 1 illustrates the process of computation of the VM. The upper panel of this figure (Fig. 1.a) shows a temporal segment of XYZ leads of the continuous HRECG record of a chagasic patient of Group III. After applying to this record the algorithms of QRS detection, alignment and averaging of sinus beats, a signal-averaged HRECG record is obtained (Fig. 1.b), which has a better signal-to-noise ratio than the original record. The individual signal-averaged XYZ leads are then filtered in order to emphasize the high frequency micropotentials and to attenuate the low frequency components (P and T waves). Following the standard recommendations [8], a 40 - 250 Hz, bidirectional, 4 order, Butterworth, band-pass filter has been used in this work. The filtered X_f, Y_f and Z_f leads (Fig. 1.c) are combined into a vector magnitude (Fig. 1.d), define as

$$VM(t) = \sqrt{X_f^{\,2}(t) + Y_f^{\,2}(t) + Z_f^{\,2}(t)} \qquad (1)$$

After calculating the VM, the onset (QRS_{on}) and offset (QRS_{off}) points of the QRS complex are estimated in the VM. A search method developed by our group [7], which employs two moving windows of variable length, is used to estimate QRS_{on} and QRS_{off}. These two points are used for the computation of three temporal indexes to detect the presence of VLP on the VM, as illustrated in Figure 2. These parameters are:

a) The total QRS duration (QRSD).

$$QRSD = QRS_{off} - QRS_{on} \qquad (2)$$

b) The root mean square voltage of the last 40 ms of the QRS (RMS40).

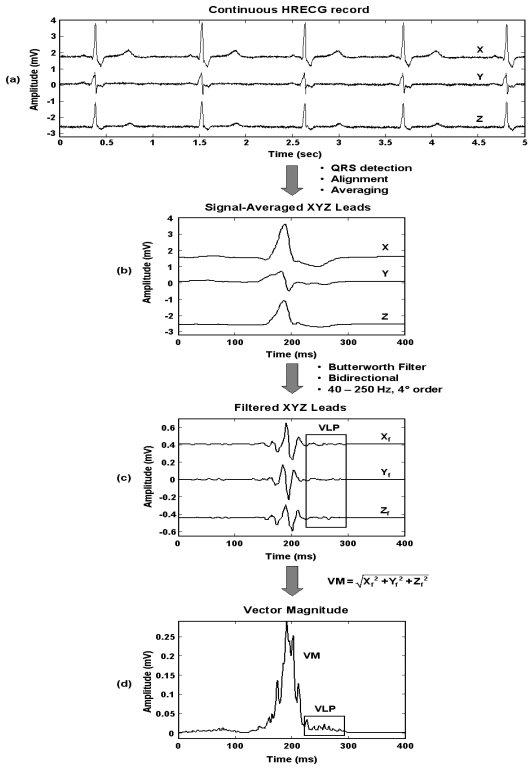

Figure 1. Computation of the vector magnitude (VM) in the temporal analysis of VLP in signal-averaged HRECG.

$$RMS40 = \sqrt{\frac{1}{T_2 - T_1} \sum_{t=T_1}^{T_2} VM^2(t)} \qquad \begin{matrix} T_1 = QRS_{off} - 40\ ms \\ T_2 = QRS_{off} \end{matrix} \qquad (3)$$

c) The duration of the terminal low amplitude signal below 40 μV (LAS40).

$$LAS40 = QRS_{off} - \operatorname{argmax}\{t \,|\, VM(t) \geq 40\mu V\} \qquad (4)$$

3.2. Beat-to-beat temporal analysis

In this analysis we had used a similar methodology to the one detailed in the previous subsection, with the difference that the technique does not use the VM of the filtered and averaged XYZ leads but rather the VM of the filtered (not averaged) XYZ leads of each sinus beat detected in the HRECG record. This technique is only

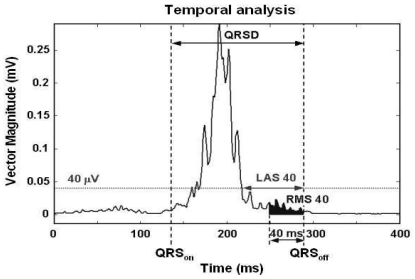

Figure 2. Indexes computed from vector magnitude in temporal analysis of signal-averaged HRECG.

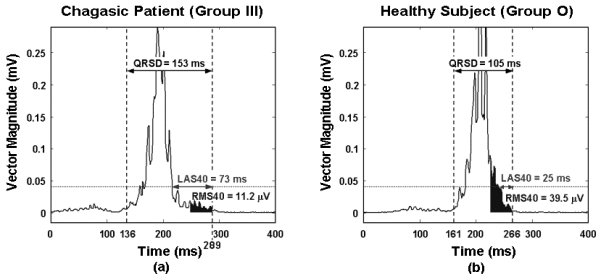

Figure 3. Signal-averaged temporal analysis for: (a) a chagasic patient of Group III, and (b) a healthy subject of Group O.

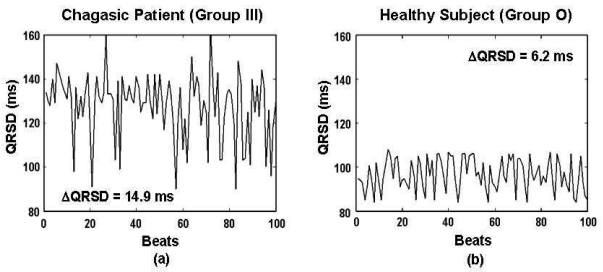

Figure 4. Beat-to-beat temporal analysis of QRSD for: (a) a chagasic patient of Group III, and (b) a healthy subject of Group 0.

used to estimate the QRSD value in each beat, since the other two parameters (RMS40 and LAS40) are greatly influenced by the noise level of the analysed beat. Once the QRSD values are estimated for all detected beats in each HRECG record, a QRSD variability index is computed as:

d) The standard deviation of beat-to-beat series of QRS duration (ΔQRSD).

$$\Delta QRSD = \sqrt{\frac{\sum_{i=1}^{n}\left(QRSD_i - \overline{QRSD}\right)^2}{n-1}} \qquad \overline{QRSD} = \frac{\sum_{i=1}^{n} QRSD_i}{n} \quad (5)$$

4. Results

The two analysis techniques described were applied to HRECG records of the 96 chronic chagasic patients (Groups I, II and III) and the 11 healthy subjects used as control group (Group O).

Figure 3 illustrates the signal-averaged temporal analysis for a chagasic patient of Group III (Fig. 3.a) and a healthy subject of Group O (Fig. 3b). Due to the presence of VLP, the chagasic patient has higher values of QRSD and LAS40, and a lower value of RMS40 (Fig. 3.a), compared with values estimated in the healthy subject (Fig. 3.b).

Figure 4 shows the beat-to-beat analysis of QRS duration for the same chagasic patient of Group III (Fig. 4.a) and the same healthy subject of Group O (Fig. 4.b), respectively. In this figure, it can be appreciated that the chagasic patient exhibits a higher standard deviation of the QRSD time series (ΔQRSD), as well as a higher mean, compared with the corresponding value in the healthy subject.

Figure 5 shows graphically the results of signal-averaged and beat-to-beat temporal analysis for the population of healthy subject (Group O) and chagasic patients (Group I, II, III). The top row of this figure (Fig. 5.a -5.d) illustrates the results of QRSD, RMS40, LAS40 and ΔQRSD indexes for each subject of all groups. The bottom row (Fig. 5.e-5.h) shows the mean and standard deviation values of each index for all subjects of each group. These last values are quantified in Table 1.

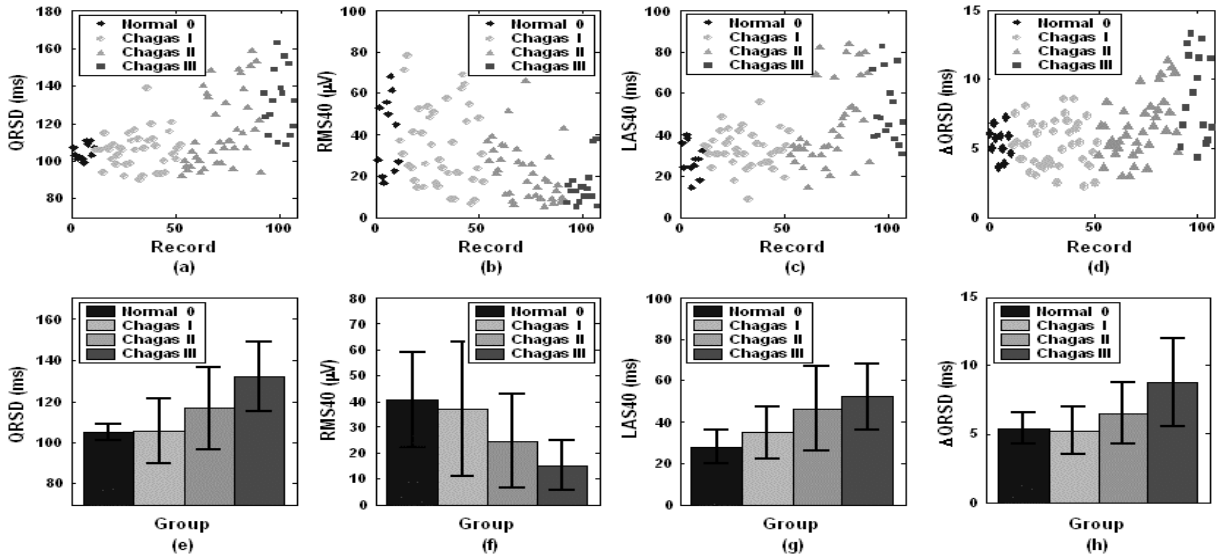

Figure 5. Results of signal-averaged and beat-to-beat temporal analysis for the populations of healthy subjects (Group 0) and chagasic patients (Groups I, II and III). Top row (a-d) illustrates the results of QRSD, RMS40, LAS40 and ΔQRSD indexes for each subject of all examined groups. Bottom row (e-h) shows the mean and standard deviation values of each index for all subjects of each group.

Index	Group O	Group I	Group II	Group III
QRSD (ms)	104.9 ± 4.2	105.6 ± 15.4	116.5 ± 20.0	131.9 ± 16.8
RMS40 (μV)	40.5 ± 18.4	37.0 ± 26.1	24.5 ± 18.1	15.1 ± 9.6
LAS40 (ms)	27.9 ± 8.1	34.7 ± 12.4	46.4 ± 20.3	52.1 ± 16.2
ΔQRSD (ms)	5.4 ± 1.1	5.6 ± 1.7	6.5 ± 2.2	8.7 ± 3.1

Table 1. Mean and standard deviation of QRSD, RMS40, LAS40 and ΔQRSD for the populations of healthy subjects (Group O) and chagasic patients (Groups I, II and III).

Table 2 presents the results of *p*-values of the Mann-Whitnney statistical test for each index when comparing two different groups. The *p*-values which are statistically significant ($p < 0.05$) have been indicated on the table with gray shading.

Index	Groups O vs I	Groups O vs II	Groups O vs III	Groups I vs II	Groups I vs III	Groups II vs III
QRSD	0.822	0.241	<0.001	0.055	<0.001	0.006
RMS40	0.364	0.012	<0.001	0.012	<0.001	0.080
LAS40	0.094	0.005	<0.001	0.015	<0.001	0.143
DQRSD	0.712	0.178	0.007	0.017	<0.001	0.011

Table 2. *P*-values of Mann-Whitnney statistical test for each index when comparing two different groups.

Finally, a VLP analysis was made using the criteria established in the standard document [8]. According to this document, a patient has VLP if QRSD> 114 ms, RMS40 < 20 μV and LAS40 > 38 ms (there is no established threshold for the parameter ΔQRSD). Table 3 shows the percentage of patients with VLP in each group.

% of patients with VLP	Group O	Group I	Group II	Group III
	0 %	12.2%	41.0%	75.0%

Table 3. Percentage of patients with detected VLP.

5. Discussion and conclusions

In this work, we have proposed the signal-averaged and beat-to-beat temporal analysis of HRECG in chronic chagasic patients with different degree of cardiac damage.

The results shown in Figure 5 and Table 1 indicate that the mean value of QRSD, LAS40 and ΔQRSD indexes increased progressively from Group O to Group III. By contrast, the mean value of RMS40 index decreased as the group number increased.

The statistical analysis shown in Table 2 reveals that two or more indexes exhibit statistical differences ($p < 0.05$) between the groups O-II, O-III, I-II, I-III and II-III. However, none of the indexes indicate statistical differences between groups O and I. This last result agrees with medical practice since the chagasic patients of the group I does not present any diagnostic evidence of myocardial damage that differentiates them from the healthy subject of group O, except for the presence of the parasite responsible for Chagas' disease.

Finally, the results detailed in Table 3 show a progressive increment of the percentage of chagasic patient with detected VLP as the group number increases, i.e. as the myocardial damage increases.

Further investigations should be carried out to examine the proposed indexes in larger populations and to establish their prognostic value in a patient classification scheme.

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