Study of the Dynamic Relationship between T Wave Morphology and Heart Rate during Ischemia

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Abstract

In this work the relationship between heart rate and several repolarization indices, including the QT interval and T wave morphology descriptors, has been investigated. A time-variant model has been proposed to describe the I_r to $\overline{RR}$ relationship, with I_r generically denoting one of the repolarization indices under study, and $\overline{RR}$ the running mean RR interval. The proposed methodology is applied to the analysis of stress test recordings. Three different groups of individuals are considered: ischemic patients, low-risk patients and healthy subjects. It is shown that the slope of the line fitting the I_r to $\overline{RR}$ beat series evaluated at stress peak is significantly lower in ischemic patients as compared to low-risk patients and healthy subjects, and that result is valid for any of the I_r indices. It can be concluded that loss of the T wave adaptation capability (lower slope) to heart rate changes, measured at stress test peak, is related of the presence of ischemia.

1. Introduction

Myocardial ischemia, which precedes infarction, is characterized by transient or permanent diminution of blood flow into the heart. Ischemia is caused by narrowing or occlusion of one or more coronary arteries. Diagnosis of myocardial ischemia is challenging, since ischemia sometimes is accompanied with pain, while other times is silent.

During the initial instants of coronary occlusion, ischemia produces changes in the ECG, mainly in the repolarization period (ST segment and T wave). Different ways of characterizing ventricular repolarization have been proposed in the literature with the aim to contribute to detect potentially arrhythmogenic abnormalities. Among those are the analysis of the QT to RR relationship [1, 2], QT interval dispersion [3] or T wave morphology descriptors [4]. In the present study we propose the quantification of the relationship between several repolarization indices, I_r, and heart rate, measured on ECG recordings of individuals performing stress test. Characteristics derived from the investigation of those relationships will be used to separate ischemic patients, low-risk patients and asymptomatic volunteers. The final purpose of our investigation is to elucidate whether ischemic patients present differential characteristics of the adaptation of repolarization to heart rate changes.

2. Methods

2.1. ECG preprocessing

The study evaluates 12-lead ECG recordings obtained from individuals while performing stress test. Preprocessing of the ECG signal includes conversion to 3-lead orthogonal configuration using the Dower matrix [5], baseline drift attenuation via cubic spline interpolation and automatic wave delineation using a multilead wavelet-based technique [6,7]. Characteristic ECG points, such as the beginning of the QRS complex and the beginning, peak and end of the T wave are obtained and they are subsequently used to compute the repolarization indices described in this section 2.2.

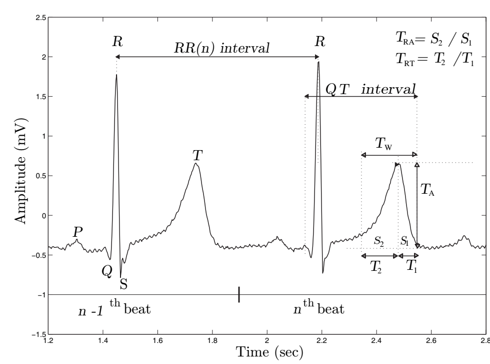

Figure 1. Representation of the repolarization indices analyzed in this study: QT interval, T wave width (T_{W}), T wave amplitude (T_{A}), ratio of the areas at both sides of T peak (T_{RA}) and ratio of the times at both sides of T peak (T_{RT}).

2.2. Repolarization indices

The repolarization indices analyzed in our study are the QT interval, the T wave width (T_{W}), the T wave amplitude

(T_{A}), two symmetry indexes defined as: the ratio of the areas at both sides of the T peak (T_{RA}) and the ratio of the T wave time expand at both sides of the T peak (T_{RT}). Those indices have been proposed in the literature and their relationship with heart rate has been established [8, 9]. A representation of such repolarization indices, which will be generically denoted by I_r, is shown in Fig.1.

For each recording, the temporal series of the following parameters are considered for the analysis: *RR* interval (measured between the R peaks of consecutive beats), *QT* interval, T_{W}, T_{A}, T_{RA} and T_{RT}, with these last five indices computed according to the definitions given in above and using the delineation marks obtained as described in Section 2.1.

To remove potential outliers from each of the measured series, a technique that uses a Median Absolute Deviation (MAD) filter is applied [10]. Subsequently, the clean series are linearly interpolated at a sampling frequency of 2 Hz and low-pass filtered (cutt-off frequency, f_c = 0.05 Hz) to remove the natural fast variability driven by the sympathetic and parasympathetic branches of the autonomic nervous system.

2.3. Time-variant model

To determine the relationship between each of the repolarization indices (I_r) and heart rate, a time-variant model with memory is proposed. The input to the model is the *RR* series, denoted by $x_{\text{RR}}(n)$, while the output is each of the analyzed repolarization indices, denoted by $y_{I_r}(n)$. There are two main reasons to propose a model with the characteristic of being time-variant. The first reason is based on the fact that the ECG signals under study are nonstationary, since they were obtained during stress test. The second reason is that the I_r to RR relationship can change during the different stages of the recording.

Figure 2 shows the proposed model, which is composed of two blocks. The first block is a 100-order time-variant FIR filter with impuse response:

$$\mathbf{h}(n) = \begin{bmatrix} h_0(n) & \dots & h_{N-1}(n) \end{bmatrix}^T \in \mathbb{R}^{N \times 1}, \quad (1)$$

whose exit is $z_{\overline{\text{RR}}}(n) = \mathbf{h}^T(n)\mathbf{x}_{\text{RR}}(n)$, where

$$\mathbf{x}_{\text{RR}}(n) = \begin{bmatrix} x_{\text{RR}}(n) & \dots & x_{\text{RR}}(n-N+1) \end{bmatrix}^T. \quad (2)$$

This first block expresses the possible dependence of the repolarization index, I_r, on a history of previous *RR* intervals. The output $z_{\overline{\text{RR}}}(n)$ represents a running weighted average of those *RR* intervals (which we denote by $\overline{RR}$). The number of coefficients of the FIR filter was defined based on previous studies [9].

The second block of the proposed model is a time-variant first-order polynomial parametrized by vector $\mathbf{a}(n)$:

$$g\left(z_{\overline{\text{RR}}}(n), \mathbf{a}(n)\right) = \mathbf{a}^T(n)\mathbf{z}_{\overline{\text{RR}}}(n), \quad (3)$$

where

$$\mathbf{a}(n) = \begin{bmatrix} a_0(n) & a_1(n) \end{bmatrix}^T \in \mathbb{R}^{2 \times 1} \quad (4)$$

and

$$\mathbf{z}_{\overline{\text{RR}}}(n) = \begin{bmatrix} 1 & z_{\overline{\text{RR}}}(n) \end{bmatrix}^T \in \mathbb{R}^{2 \times 1}. \quad (5)$$

This second block expresses how the repolarization index, I_r, evolves as a function of the averaged RR measurement obtained at the output of the FIR filter.

A constraint is imposed in the determination of the two blocks which guarantees uniqueness of the solution. The constraint is such that the sum of all the coefficients of the time-variant FIR filter is 1: $\mathbf{h}^T(n)\mathbf{1} = 1$ with $\mathbf{1}$ denoting the N x 1 vector of ones. Also, the coefficients of the linear filter are constrained to be positive, so as to be able to derive meaningful physiological interpretations.

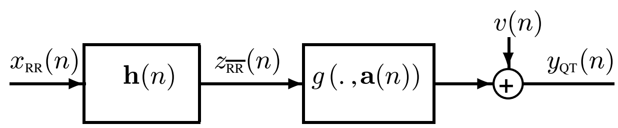

Figure 2. Two-block time-variant model proposed to investigate the I_r to RR relationship. The input is the *RR* series and the output is one of the I_r indices, e.g the QT interval in the plot.

Additionally, white gaussian noise, $v(n)$, uncorrelated with the input signal, $x_{\text{RR}}(n)$, is added at the output of the global system. That noise accounts both for delineation errors, generated when the repolarization index is measured, and modelling errors due to the assumption of the proposed model. Consequently, the output of the model is expressed as:

$$y_{I_r}(n) = \mathbf{a}^T(n)\mathbf{z}_{\overline{\text{RR}}}(n) + v(n). \quad (6)$$

To perform the estimation and identify the unknown parameters of the proposed model, we consider a unique vector $\boldsymbol{\theta}(n)$ that gathers all of the parameters in $\mathbf{h}(n)$ and $\mathbf{a}(n)$. That vector $\boldsymbol{\theta}(n)$ is defined as:

$$\boldsymbol{\theta}(n) = \begin{bmatrix} a_0(n) & a_1(n)\mathbf{h}^T(n) \end{bmatrix}^T \in \mathbb{R}^{(N+1) \times 1}. \quad (7)$$

The output of the system can thus be expressed as a function of the input vector $\mathbf{x}_{\text{RR}}(n)$ and the parameter vector $\boldsymbol{\theta}(n)$ using the following expression:

$$y_{I_r}(n) = \mathbf{f}_{\text{RR}}(n)\boldsymbol{\theta}(n) + v(n), \quad (8)$$

where $\mathbf{f}_{\text{RR}}(n) = [1 \;\; \mathbf{x}_{\text{RR}}(n)]^T$.

The adaptive methodology used for the estimation is based on the Kalman filter. Before applying the Kalman Filter, a state-space representation of the model described in equation (8) is formulated. Regularization is incorporated into that representation so as to deal with the "ill-posed" condition of the problem to be solved. Such a regularization process prevents the solution from fluctuating excessively in the presence of disturbances affecting the output of the unknown system [9].

2.4. Risk stratifiers

The slope value of the line that fits the $[z_{\overline{RR}}(n'), y_{l_r}(n')]$ data pairs in a small neighbourhood of time instants n' around n is $a_1(n)$, and from here will be denoted as $\lambda(n)$, $a_1(n) \equiv \lambda(n)$, and proposed as a potential risk stratifier.

In this study, $\lambda(n)$ is evaluated at three different stages of the stress test [11], which are shown in the top panel of Fig. 3. The first analysis interval is denoted by P_1 and comprises the initial 2 minutes of the test. The second interval, P_2, covers the 2 minutes ending just before the stress peak. Finally, the third interval is denoted by P_3 and is defined to cover the 2 minutes starting 30 seconds after the stress peak. The mean value of $\lambda(n)$ across each of those intervals is denoted by λ_{P_j}, with j = 1, 2, 3.

2.5. Statistics

The variable λ_{P_j} evaluated on individual recordings is compared for individuals in each of the three groups that will be described in Section 3. Student's two-tail two-sample t-test assuming unequal variances is used. A p-value < 0.05 is considered as statistically significant.

3. Database

The data population is composed of 143 ECG recordings obtained from patients undergoing stress test at the Lozano Blesa University Hospital, Zaragoza (Spain). Of the total number of patients, 65 are classified as ischemic (positive stress test and coronary angiography), 38 are classified as low-risk (negative stress test and Framingham index lower than 5% [11]) and 40 are asymptomatic volunteers. The three groups are denoted by I (ischemic), LR (low-risk) and A (asymptomatic).

The mean±standard deviation age of the database is 45±13.36 years. There are 12 women and 131 males.

4. Results

Fig.3 shows an example corresponding to one of the recordings analyzed in this study. The top panel of that figure shows the $x_{RR}(n)$ series, the middle panel shows the $y_{QT}(n)$ interval series, and the botton panel presents the values of the variable $\lambda(n)$ evaluated along the recording.

Fig. 4 shows mean $\pm$ standard error of the mean for each of the slopes λ_{P_j} (j = 1, 2, 3) calculated from optimally fitting the QT and T_w to $\overline{RR}$ relationship using a linear polynomial. The values of λ_{P_j} are calculated separately for each of the three groups described in Section 3. From fig. 4 it can be observed that the slope values corresponding to ischemic patients are clearly inferior to those corresponding to low-risk patients and asymptomatic subjects.

For the other analyzed repolarization indices, T_A, T_{RA} and T_{RT}, the tendency shown for QT and T_w is not always observed: the differences between ischemic patients and the other two groups (low-risk patients and asymptomatic subjects) are less manifested in most cases. The tendency can be seen in table 1.

Results obtained from the Student's t-test for group separation using the variable λ_{P_2} (just before stress peak) are presented next in table 1. It can be concluded that separation is statistically significant when distinguishing the ischemic group from the other two groups, low risk and asymptomatic, both for the analysis of the QT interval and for that of the T wave width (T_w).

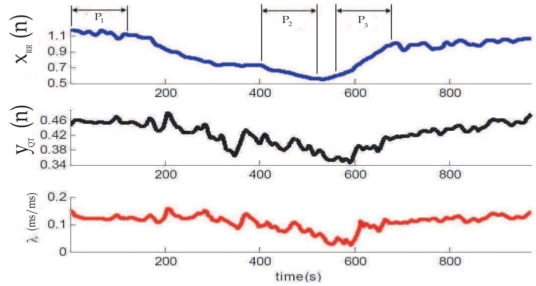

Figure 3. Temporal series measured along the stress test for a particular recording of the study population. Top panel: $x_{RR}(n)$ interval series, middle panel: $y_{QT}(n)$ interval series, and bottom panel: slope $\lambda(n)$. The intervals P_1, P_2 and P_3 (described in Section 2.4) are marked in the top panel.

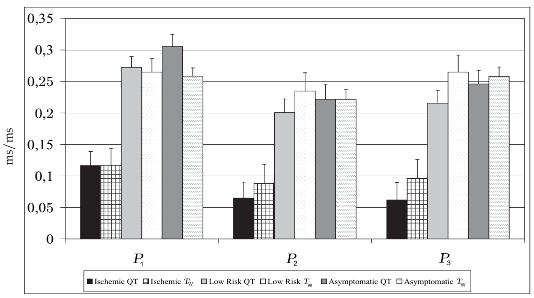

Figure 4. Mean $\pm$ standard error of the mean for the variables λ_{P_j} with j = 1, 2 and 3, when the studied index are the QT interval and T width T_w.

5. Discussion and conclusions

A dynamic model has been proposed to investigate the relationship between heart rate and diverse repolarization

	λ_{P_2} (ms/ms)			p values		
I_r	I	LR	A	LR vs A	I vs LR	I vs A
QT	0.06 $\pm$ 0.20	0.20 $\pm$ 0.13	0.22 $\pm$ 0.15	0.5140	0.0004	$5.97 \cdot 10^{-5}$
T_{W}	0.09 $\pm$ 0.24	0.23 $\pm$ 0.18	0.22 $\pm$ 0.10	0.6880	0.0014	0.0011
T_{A}	-0.83 $\pm$ 1.74	-2.66 $\pm$ 2.40	-0.63 $\pm$ 2.45	0.0004	$1.92 \cdot 10^{-5}$	0.6250
T_{RA}	0.13 $\pm$ 3.06	-0.02 $\pm$ 2.75	-0.55 $\pm$ 2.77	0.4000	0.8020	0.2540
T_{RT}	0.48 $\pm$ 4.09	-0.80 $\pm$ 2.87	-0.53 $\pm$ 3.23	0.7050	0.0930	0.1850

Table 1. Table showing, in the first three columns, the mean values of λ_{P_2} for the repolarization indices for the different groups of persons (I, LR and A), and, in the last three columns, the p values for distinguishing between the different groups for the repolarization descriptors, all for λ_{P_2}.

indices including the QT interval and T wave morphology descriptors. The proposed models accounts for the influence of a history of previous RR intervals on each repolarization measurement and it is able to follow the rate-dependency of repolarization descriptors on a beat-to-beat basis.

The dynamicity of the model is particularly important for the analysis of stress test recordings, which have the characteristic of being highly nonstationary. In this study, our methodology has been applied to differentiate repolarization characteristics evaluated during stress test for three different groups of individuals: ischemic patients (positive stress test and positive coronarography), low-risk patients (negative stress test and Framingham index $< 5\%$), and asymptomatic subjects. Measuring the slope of the line that fits the I_r to $\overline{RR}$ relationship for the analyzed repolarization indices (QT, T_{W}, T_{A}, T_{RA}, T_{RT}), we have demonstrated that rate-dependence of repolarization is significantly different for ischemic patients as compared to low-risk patients and asymptomatic subjects. Specifically, we have shown that ischemic patients have considerably reduced slopes of the I_r to $\overline{RR}$ relationship, particularly when measured for I_r = QT or T_{W} (the T_{A}, T_{RA} and T_{RT} are measured not a any particular lead, but at the lead where the higher signal to noise ratio of the T wave projection is obtained, and this can vary from patient to patient [7]).

Our results point out that loss in the capability of T wave adaptation to heart rate changes (lower slope of the I_r to $\overline{RR}$ relationship at stress peak) can be indicative of the presence of ischemia.

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