Assessing QT-RR Interval Hysteresis in 12-Lead Electrocardiograms

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Abstract

The amount of QT-RR interval hysteresis accumulated during the load and recovery phases of exercise stress test reflects the degree of exercise induced myocardial ischemia. Therefore the evaluation of hysteresis from 12-lead ECG (12-SL) is an important practical modality for the assessment of severity of coronary artery disease. Commercial QT and RR waveform analyzers are regularly subjected to interval detection artifacts which prevent reliable estimation for the magnitude of QT-RR hysteresis in one or multiple leads. We present a new signal processing technique which overcomes this deficiency. It quantifies the level of faulty interval measurements and using a threshold eliminates the need to process potentially corrupt leads.

1. Introduction

During physiological exercise the adaptation rate of low frequency QT interval dynamics falls behind the corresponding changes of RR intervals. These lag-type interval changes manifest themselves in the form of QT-RR interval hysteresis which progressively accumulates during the load and recovery stages of an exercise test. Several clinical and experimental studies have previously confirmed that stronger myocardial ischemia and coronary artery disease are associated with higher magnitude of QT-RR hysteresis [1–3]. However, due to noisy ECG signals and subsequent irregularities of the QT-RR interval measurements the magnitude of QT-RR hysteresis can be significantly distorted. Inconsistent QT-RR interval measurements may complicate the interpretation of QT-RR interval hysteresis and overshadow its underlying dynamics in one or multiple leads.

In this paper we suggest a computerized lead selection algorithm which improves reliability of QT-RR hysteresis calculation. Unlike previously implemented methods [4, 5], our approach naturally incorporates dynamics of physiological exercise and readily accounts for the lag-type time dependence of QT interval on RR interval history which develops in response to changes in exercise load [6, 7].

2. Method of lead selection

Our approach is based on tracking the level of noise in QT intervals which are not influenced by physiological RR interval variability. We model short term QT interval sequences as outputs of a linear filter with recent RR interval as input sequences (Eq. 1). The sequences of QT and RR intervals are obtained by linearly interpolating their unevenly sampled measurements at sufficiently high frequency.

$$QT(i) = \sum_{j=i-M+1}^{j=i} w(i-j)RR(j) + u(i) \qquad (1)$$

where filter's length M determines duration of RR interval history, $w(k), (1 \leq k \leq M)$ are filter coefficients and u is the random component of QT interval variability attributed to both detection artifacts and noisy measurements. The output of filter $\mathbf{w}$ determines QT interval component which is correlated with RR variability. On the contrary, component u contributes only to the uncorrelated variability of QT interval response.

In order to determine the function $\mathbf{w}$, we employ a method based on the adaptive Least Mean Square (LMS) algorithm [8]. The course of active exercise (excluding rest) is separated into $N = D_T/K_T$ short term adaptive stages, where D_T is the duration of entire exercise, and K_T is the adaptive period during which the function $\mathbf{w}$ is identified.

An approximation $\hat{\mathbf{w}}_m$ to the unknown filter $\mathbf{w}$ is ascertained for every adaptive stage $m = 1, 2..., N$. Each approximation to the filter $\mathbf{w}$, $\hat{\mathbf{w}}_m$, determines the component of QT interval measurements, QT_e, which is correlated to RR intervals within each adaptive stage m. This is equivalent to minimizing the mean square of the estimation error, $||QT - QT_e||_{L_2}$.

QT_e estimates were determined for the entire duration of exercise by implementing filter (1) for each adaptive stage. For every lead, we computed the average norm L_2 over the interval D_T . The value of this norm quantified the level of uncorrelated QT interval variability.
The lead with the smallest L_2 norm L_{min} was considered as the best quality lead with minimal level of noise. A subset of leads with a normalized difference $L_{norm} = \frac{L-L_{min}}{L_{min}}$ smaller than a certain threshold (noise tolerance factor) was selected for evaluation of QT-RR hysteresis. A median value of QT-RR hysteresis computed for each subset was used as the outcome of an exercise test. Iterative steps describing the filter adaptation process for any adaptive stage m are given below,

$$\begin{aligned} \text{Initialization: } \hat{\mathbf{w}}_m &= \mathbf{0} \\ \text{Iterations: for } n &= 1, 2, 3, ...K \\ e(n) &= QT(n) - \hat{\mathbf{w}}_m^T \mathbf{RR(n)} \\ \hat{\mathbf{w}}_m(n+1) &= \hat{\mathbf{w}}_m(n) + \mu e(n) \mathbf{RR(n)} \end{aligned}$$

Here $QT(n)$ and $RR(n)$ are evenly resampled QT and RR signals, $\hat{\mathbf{w}}_m(n)$ is the filter estimate at sample time n, and $\mathbf{RR(n)}$= $[RR(n), RR(n-1), ..., RR(n-1+M)]$ is a vector of M recent RR intervals. K is the number of samples in each adaptation stage and μ is the adaptation constant. Choosing parameters M, K_T and μ remains a heuristic task that needs to address several aspects of the problem. Main trade-off is between smoothing capacity of the filter and computational efficiency within each adaptation stage on one hand and overall QT-RR interval dynamics that results in hysteresis on the other hand.

3. Results

Our study group consisted of patients enrolled in the outpatient clinic of East Carolina Heart Institute at East Carolina University. A goal of the study was to assess the level of exercise induced ischemia implementing a novel quasi-stationary exercise test. Speed and elevation of the GE treadmill belt were changed every minute using a gradual quasi-stationary exercise protocol [1]. A research version of the GE Healthcare Clinical Systems CASE 8000 software (GE Workstation 1.8) allowed us to export beat-to-beat QT and RR interval measurements in ASCII format. Beat-to-beat QT interval measurements were available in all 12 leads, while RR interval measurements were represented by a single data set which was the same for all leads. The ASCII interval data sets were used for subsequent post processing using the Matplotlib software package in Python.

After resampling at 7 Hz, resampled signals $QT(n)$ from each lead and the common $RR(n)$ signal were analyzed using the Lead Selection Process described in a previous section. The value of adaptive period K was equal to 84 samples which allowed us to update filter approximation $\hat{\mathbf{w}}_m$ every 12 seconds ($K_T = 12$). The depth of RR interval history incorporated in Eq. 1 was one second ($M = 7$). The adaptation constant μ was set to 0.3. These parameters were chosen based on our observations that the period of physiological correlation between QT and RR intervals were longer than 10 seconds.

Low frequency QT and RR interval trends were obtained by applying a low pass filter with a cutoff frequency of 0.008 Hz to $QT(n)$ and $RR(n)$ signals, respectively. Typical examples of decreasing and increasing series of RR intervals collected during a quasi-stationary exercise test are shown in Fig. 1. Corresponding QT interval signals from all 12 leads are displayed in Fig. 2. While RR interval history is ideally correlated with QT interval dynamics in V_4 ($L_{norm} = 0$), it has insufficient correlation with QT intervals in the lead aVL due to a high level of random noise characterized by $L_{norm} = 6.17$. We observed that using a sufficiently low noise tolerance factor of $L_{norm} = 0.2$ allowed us to separate leads with excessive noise from those suitable for evaluation of QT-RR hysteresis. After lead selection with this threshold faulty leads in Fig. 2 were eliminated and only left and one right precordial leads were used for hysteresis evaluation (Table 1).

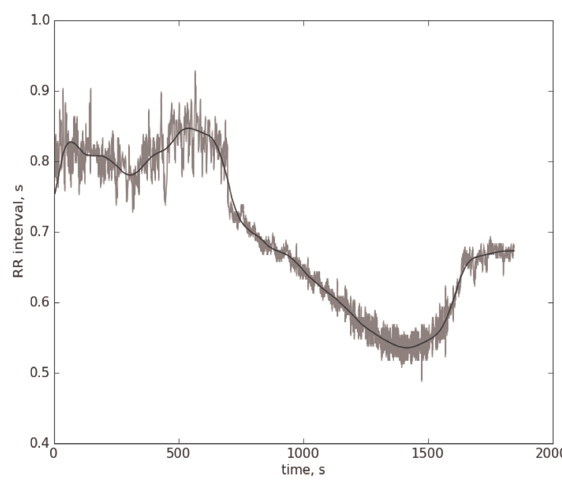

Figure 1. RR interval sequence. Resampled signal $RR(n)$ is shown in gray , low frequency trend in black.

Figure 3 shows the hysteresis curve inscribed by QT and RR interval trends for the lead V_4 in Fig. 2. The hysteresis loop is closed by a vertical line at ninety-five percent of the post recovery RR interval value. The magnitude of hysteresis (hysteresis index) is determined as the area of this loop normalized by the area of the bounding rectangular box.

Table 1 shows hysteresis indices evaluated for the case depicted in Fig. 2. All selected leads are indicated by bold letters. Index values in different leads vary significantly (217-356) which complicates choosing a single value or computing the median estimate for QT-RR hysteresis. Selected leads with a low noise tolerance factor provide more dependable median index (249) from a tighter range of values (217-264). Fig. 4 shows another example in which most leads except aVL and V_1 have satisfactory recordings ($L_{norm} < 0.3$). Leads aVL and V_1 display higher levels of noise ($L_{norm} > 0.5$) near the peak and beginning of exercise, respectively . Although hysteresis index in these two leads differs by a factor of 2, the selected leads (Table 2) are characterized by much smaller index variability and provide more accurate evaluation of the median hysteresis value.

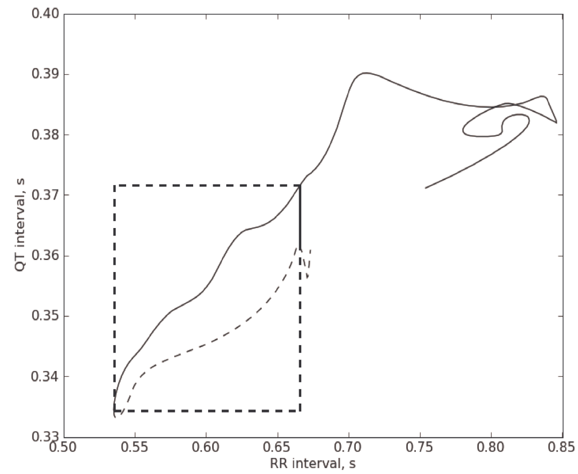

Figure 3. Accumilation of QT-RR hysteresis between the load (solid curve) and recovery stages (thin dashed curve) of the QT-RR curve. A solid vertical line superimposed on the side of the bounding box (thick dashed lines) marks the closure of the loop.

4. Conclusions

In this paper we have described a robust approach for assessing QT-RR interval hysteresis index using body surface 12 lead ECG recordings. Our lead selection algorithm is an effective tool for detection of noisy leads and can be used to improve reliability and consistency of hysteresis index computations. The algorithm can be readily integrated into the existing waveform analyzers and used in clinical studies to minimize interpretation errors. Our method can be also extended for short and long term analyses of the QT-RR interval profiles collected during ambulatory ECG recordings at rest.

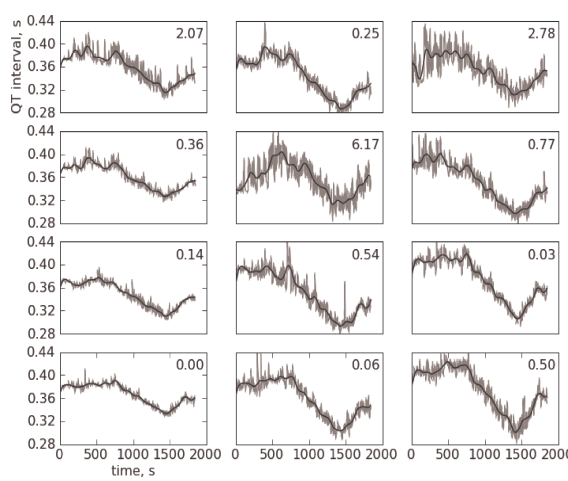

Figure 2. 12- SL QT intervals (Example 1). Each panel shows $QT(n)$ in gray and its low frequency trend in black. Lead names in a row-wise manner are I, II, III, aVR, aVL, aVF, V_1, V_2.., V_6. Corresponding L_{norm} is displayed at the upper right corner of each panel.

Table 1. Hysteresis distribution in example 1.

Lead	I	II	III
Hysteresis	336	267	322
Lead	aVR	aVL	aVF
Hysteresis	332	304	273
Lead	**V_1**	V_2	**V_3**
Hysteresis	246	356	264
Lead	**V_4**	**V_5**	V_6
Hysteresis	252	217	222

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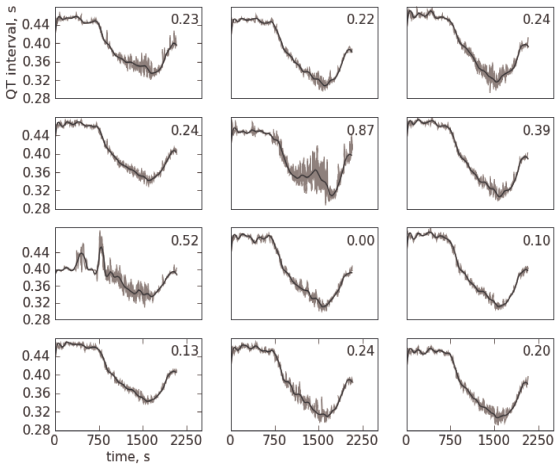

Figure 4. 12- SL QT intervals (Example 2). Each panel shows $QT(n)$ in gray and its low frequency trend in black. Lead names in a row-wise manner are I, II, III, aVR, aVL, aVF, V_1, V_2.., V_6. Corresponding L_{norm} is displayed at the upper right corner of each panel.

Table 2. Hysteresis distribution in example 2.

Lead	I	II	III
Hysteresis	246	232	196
Lead	aVR	aVL	aVF
Hysteresis	227	278	237
Lead	V_1	$\mathbf{V}_2$	$\mathbf{V}_3$
Hysteresis	123	184	181
Lead	$\mathbf{V}_4$	V_5	$\mathbf{V}_6$
Hysteresis	198	225	232

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