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.

\[ QT(i) = \sum_{j=M+1}^{j=i} w(i-j)RR(j) + u(i) \] (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 \( w \) 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 \( w \), 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 \( w \) is identified.

An approximation \( \hat{w}_m \) to the unknown filter \( w \) is ascertained for every adaptive stage \( m = 1, 2, ..., N \). Each approximation to the filter \( w, \hat{w}_m \), determines the component of QT interval measurements, \( QT_m \), which is correlated to RR intervals within each adaptive stage \( m \). This is equivalent to minimizing the mean square of the estimation error, \( \|QT - QT_m\|_{L_2} \).
The lead with the smallest $L_2$ norm $L_{\text{min}}$ was considered as the best quality lead with minimal level of noise. A subset of leads with a normalized difference $L_{\text{norm}} = \frac{L_0 - L_{\text{min}}}{L_{\text{min}}}$ 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,

Initialization: $\hat{w}_m = 0$

Iterations: for $n = 1, 2, 3, \ldots K$

\[
\hat{w}_m(n + 1) = \hat{w}_m(n) + \frac{1}{n} \left[ QT(n) - \hat{w}_m(n) \right]
\]

Here $QT(n)$ and $RR(n)$ are evenly resampled QT and RR signals, $\hat{w}_m(n)$ is the filter estimate at sample time $n$, and $RR(n) = [RR(n), RR(n-1), ..., RR(n-1+M)]$ is a vector of $M$ recent RR intervals. $K$ is the number of samples in each adaptation stage and $\mu$ is the adaptation constant. Choosing parameters $M$, $K_T$ and $\mu$ 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 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 $K_T$ was equal to 84 samples which allowed us to update filter approximation $\hat{w}_m$ every 12 seconds ($K_T = 12$). The depth of RR interval history incorporated in Eq. 1 was one second ($M = 7$). The adaptation constant $\mu$ 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 $V_4$ ($L_{\text{norm}} = 0$), it has insufficient correlation with $QT$ intervals in the lead aVL due to a high level of random noise characterized by $L_{\text{norm}} = 6.17$. We observed that using a sufficiently low noise tolerance factor of $L_{\text{norm}} = 0.2$ 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.](image.png)

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 V₁ have satisfactory recordings (Lnorm < 0.3). Leads aVL and V₁ display higher levels of noise (Lnorm > 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.

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.

Table 1. Hysteresis distribution in example 1.

<table>
<thead>
<tr>
<th></th>
<th>I</th>
<th>II</th>
<th>III</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hysteresis</td>
<td>336</td>
<td>267</td>
<td>322</td>
</tr>
<tr>
<td>Lead</td>
<td>aVR</td>
<td>aVL</td>
<td>aVF</td>
</tr>
<tr>
<td>Hysteresis</td>
<td>332</td>
<td>304</td>
<td>273</td>
</tr>
<tr>
<td>Lead</td>
<td>V₁</td>
<td>V₂</td>
<td>V₃</td>
</tr>
<tr>
<td>Hysteresis</td>
<td>246</td>
<td>356</td>
<td>264</td>
</tr>
<tr>
<td>Lead</td>
<td>V₄</td>
<td>V₅</td>
<td>V₆</td>
</tr>
<tr>
<td>Hysteresis</td>
<td>252</td>
<td>217</td>
<td>222</td>
</tr>
</tbody>
</table>

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References

Table 2. Hysteresis distribution in example 2.

<table>
<thead>
<tr>
<th>Lead</th>
<th>I</th>
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<tbody>
<tr>
<td>Hysteresis</td>
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<td>232</td>
<td>196</td>
</tr>
<tr>
<td>Lead</td>
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<td>aVF</td>
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<tr>
<td>Hysteresis</td>
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<td>237</td>
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<tr>
<td>Lead</td>
<td>V₁</td>
<td>V₂</td>
<td>V₃</td>
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<tr>
<td>Hysteresis</td>
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</tr>
<tr>
<td>Lead</td>
<td>V₄</td>
<td>V₅</td>
<td>V₆</td>
</tr>
<tr>
<td>Hysteresis</td>
<td>198</td>
<td>225</td>
<td>232</td>
</tr>
</tbody>
</table>

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, V₁, V₂, V₆. Corresponding $L_{norm}$ is displayed at the upper right corner of each panel.


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