Stability of QT Measurements in the PTB Database Depending on the Selected Lead

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Abstract

Prolonged QT interval is considered as an index of propensity to dangerous ventricular tachyarrhythmias. The Physionet/CinC challenge 2006 encourages teams to automatically measure the QT interval of lead II's first representative beat in every record of the PTB database. A "median self-centering approach" based on manual entries to the challenge is used for evaluation of algorithms.

We participated in the challenge using a single-lead wavelet based delineator. The selection of the representative beat was performed using information from several beats and the available leads. A score of 19.22 ms was obtained. Additionally the stability of the delineation in the different leads is studied. Comparing the QT measurement stability in 10 consecutive beats, we found significant inter-lead differences. The most stable QT measurements were found in precordial leads V2-V4, while frontal leads are those with greatest measurement variance. Leads with more stable QT were also those with maximum T wave amplitude.

1. Introduction

Prolonged cardiac repolarization is associated with propensity to ventricular tachyarrhythmias, such as torsade de pointes, which may degenerate into malignant arrhythmias such as ventricular fibrillation. This phenomenon is manifested in the electrocardiogram (ECG) as a prolongation of the QT interval, which represents the total duration of ventricular depolarization and repolarization in a cardiac cycle. Despite the suggested limitations [1], the QT interval remains the most widely used index for assessing the susceptibility to ventricular arrhythmias.

Prolonged cardiac repolarization can be caused by a congenital disease (e.g. Long QT syndrome) or acquired. Certain drugs have the ability to prolong myocardial repolarization [2], which motivated regulatory actions. Drug regulatory agencies including US FDA, the European Mecicines Agency or Japan's National Institute of Health Services have adopted the ICH E14 guidelines, which require the accomplishment of so-called "thorough QT/QTc studies" [3].

Presently, automatic QT interval measurements are not considered reliable enough to be used in these studies. However, manual delineation, even in ECG laboratories, is not fully reliable as discussed in [1].

The Physionet/CinC Challenge 2006 encourages participants to develop methods for automatic QT measurement in a "representative" beat in the lead II of the 549 records of the PTB database (PTBDB). The validation of the methods is based on the median of manual or semi-automatic measurements submitted by participants in Division 1 of the challenge [4].

In this paper, we describe our participation in Division 2 of the Physionet/Cinc Challenge 2006, using a previously developed wavelet-based ECG delineator [5] and study the beat-to-beat stability of the delineation depending on the selected lead.

2. Materials and methods

2.1. Database

The PTB diagnostic ECG database (PTBDB) [6, 7], available in www.physionet.org consists in 549 records from 294 subjects. Each record contains the standard 12-lead ECG and the simultaneously recorded 3 Frank lead ECG. The signals are sampled at 1000 Hz, with a resolution of 0.5 μV and have variable duration. The database includes 54 healthy controls as well as patients with different pathologies.

2.2. ECG delineation

In this work we have used a multiscale wavelet-based ECG delineator previously developed and validated by the authors [5]. In this method, the discrete wavelet transform is applied to the ECG signal, using a quadratic spline wavelet. Due to the characteristics of quadratic spline, the wavelet coefficients are equivalent to the derivative of the ECG signal smoothed at different scales.

The algorithm searches then the maxima and minima

of the differentiated signals at different scales, detecting and classifying the significant slopes of the signal. The scales analyzed are different for waves with different spectral content (e.g. for QRS and T wave delineation).

According to the number and polarity of the significant slopes, the algorithm labels the individual waves of the QRS and classifies the T waves as positive, negative, biphasic, only upwards or only downwards. Finally, a multiscale threshold approach is used to locate the waveform limits.

2.3. Strategy for beat selection

Due to the challenge design, the selection of a representative beat plays a fundamental role in the outcome.

Our strategy is based in the following ideas: a) The representative beat, the previous and the subsequent beat should not be premature or ectopic beats. b) The QT of the representative beat measured in lead II should not be an outlier with respect to the QT in the rest of leads. c) The representative beat must have a QT measurement near the median QT in the neighborhood.

These ideas are implemented as follows when analyzing each record:

- Delineation of the first 30 seconds in the 12 standard leads. A QRS onset and a T wave end (if a T wave is detected) are determined for each beat and lead. When both QRS onset and T wave end annotations are available, a QT interval is computed.
- Records with less than 75% delineated T waves within the first 30 seconds of the desired lead (lead II for the Challenge) were not considered for the analysis (usually due to negligible T wave amplitude in that lead).
- Premature beats, as well as the previous and following beats are considered as non-valid for QT measurement. A beat was considered premature if its previous RR was lower than 80% of the median RR .
- Beats with QTc > 520 ms or QTc < 340 ms are considered non-valid.
- A global QRS onset and a global T wave end was computed for each beat using the annotations of the 12 leads. For that purpose, the QRS onsets and T-wave ends of the different leads are sorted (a maximum of 12 for each of the two limits). Then, the global QRS onset is defined as the earliest QRS onset in any lead followed by at least 3 other onsets in the subsequent 12 ms. Similarly, the last T-wave end preceded by at least 3 other ends in the previous 12 ms is considered to be the global T-wave end. This multilead delineation rule has been previously used in [5]. When possible, a global QT was computed as the interval between the global QRS onset and the global T-wave end.
- Beats whose QT interval measured in the desired lead was more than 5 ms larger or more than 100 ms shorter than the global QT were considered as non-valid measurements and excluded for further analysis.
- A *representative* QT (QTrep) was computed as the median of the valid QT measurements within the first 30 seconds of the desired lead.
- The representative beat was selected as the first valid beat whose QT in the desired lead is within a 10-ms difference of QTrep. If no beat satisfies this condition, the first beat with a QT within a 20-ms difference of QTrep is searched. If this condition is not satisfied, no QT is supplied for that record.

2.4. QT measurement stability

The stability of QT measurements has been quantified in each lead as the standard deviation of measured QT intervals in 10 consecutive non-ectopic beats s_{QT10}. For that purpose, the earliest run of 10 or more beats with stable RR interval (beats whose RR intervals do not differ from the median RR in more than 20% of the median RR) has been selected. The values of s_{QT10} include mainly physiological beat-to-beat repolarization variability, QT variations associated to changes in the heart electrical axis (e.g. due to respiration) as well as delineator variability. Additionally the beat-to-beat standard deviation of the intervals from QRS fiducial point to QRS onset and T wave end annotations were also computed in the same run of beats ($s_{QRSon10}$ and s_{Tend10}).

The mean T wave amplitude T_{amp} in each lead and the mean T wave electrical vector in the same set of 10 stable beats were also measured to help understanding the differences in QT measuremente stability.

3. Results

3.1. Validation with manual or semiautomatic annotations

An entry was submitted to the Physionet/CinC challenge 2006 applying the wavelet-based delineator described in [5] and the beat selection strategy described in Section 2.3. The final submitted entry supplied a QT in 525 records (95.63 %). The mean measured QT in the database was 377.9 ms $\pm$ 38.0 ms (mean $\pm$ std. dev.). The final score in the challenge was 19.22 ms. According to the scoring method, this means that the RMS value of the difference between our QT measurements and the reference QT intervals (the median of the manual and semiautomatic entries to the challenge) was of 18.38 ms.

Shortly after the deadline of the Challenge, the reference QT intervals were published. According to these data, our entry had a bias of -4.0 ms and a standard deviation of 17.9 ms. Figure 1 shows a cumulated histogram of the absolute errors with respect to the reference QT. A Bland-Altman

plot showing the differences between measured and reference QT is given in Figure 2.

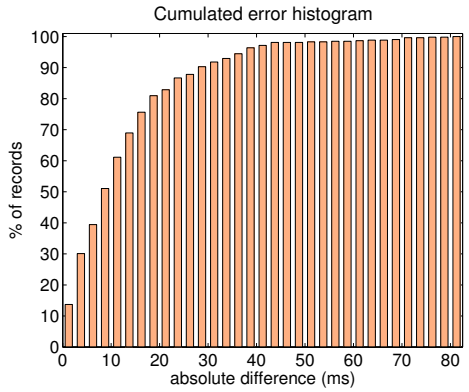

Figure 1. Cumulated distribution of the absolute difference between QT measured in lead II and reference QT.

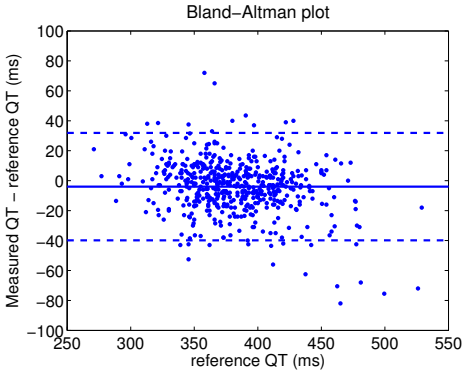

Figure 2. Bland-Altman plot of the measurement errors in lead II with respect to the challenge's reference QT.

We obtained QT measurements in all the leads by applying the same beat selection strategy described in Section 2.3 to every available lead. Table 1 shows the differences of the QT measured in every lead with respect to the QT references.

An additional set of reference manual QT annotations in the PTBDB was recently published by Christov *et al.* [8]. They were generated from the annotations of four cardiologists and a biomedical engineer, with similar instructions as those of the Physionet/CinC challenge (the main differences being that all cardiologists annotated the same beat, and they were asked to look for a global QT measurement if T wave was not clear in lead II). With respecto to those annotations, our challenge entry had a mean QT difference of -0.5 ms and a standard deviation of 19.2 ms.

3.2. QT measurement stability

A sequence of more than 10 stable beats as described previously was found in 505 records (92%). Figure 3 shows the box and whiskers plots for the stability of the measurements of QRS onset (a), T wave end (b) and QT (c). The distribution of T wave amplitude in the the 15 available leads is also shown in Figure 3(d).

Table 1. Bias and standard deviation of QT measurement with the proposed procedure in all the available beats with respect to reference annotations of the challenge.

Lead	ΔQT (ms)	Lead	ΔQT (ms)	Lead	ΔQT (ms)
aVL	-5.5±22.4	V_1	-8.0±26.1	X	-4.7±23.6
I	-3.7±22.7	V_2	-5.1±24.0	Y	-3.0±19.0
-aVR	-4.9±22.0	V_3	-1.8±23.0	Z	-2.7±23.0
II	-4.0±17.9	V_4	-2.6±23.7		
aVF	-3.1±19.8	V_5	-6.3±24.4		
III	-4.1±21.5	V_6	-5.3±23.2		

Regarding the T wave electrical vector, the mean axis through the database has an angle of 48^o with respect to X axis in the frontal plane. In the transversal plane, the angle is -62^o with respect to X axis (pointing between the directions of standard leads V3 and V4).

4. Discussion and conclusions

An automatic QT analyzer has been presented based on a single-lead wavelet-based delineator plus a set of rules for selecting a representative beat. With a score of 19.22 ms, it was one of the three automatic methods with score below 20 ms [4].

The QT measurements supplied by the proposed technique have a slight bias (-4.0 ms), with a standard deviation of 17.9 ms. Figure 1 shows that 51% of records had a QT error lower than 10 ms, and 81% of records measured a QT within 20 ms of the reference QT. The Bland-Altman plot (Figure 2) does not show clear trends in the QT error. Only in some records with QT>450 ms, the measurement tends to underestimate the QT interval.

QT measurement stability was found to be very different from lead to lead. Leads with most stable QT delineation were V2, V3 and V4 with mean (median) s_{QT10} values of 8.2 ms (2.5 ms), 8.1 ms (2.3 ms) and 9.0 (2.9 ms). QT measured in frontal leads are the least stable. Lead II, one of the most used for QT quantification had a mean s_{QT10} of 20.9 ms (median: 8.0 ms). Since the physiological repolarization variability does not depend on the lead, such inter-lead differences can be attributed to measurement variability (which is expected to be lower in leads with greater signal-to-noise ratio) and/or the different sensitivity of the leads to beat-to-beat rotations of the electrical axis (e.g. owing to respiration). The main component of the beat-to-beat variations is due to T wave end stability. Leads with most stable T wave end, and therefore QT measurements are those with largest T waves and best projection of the T

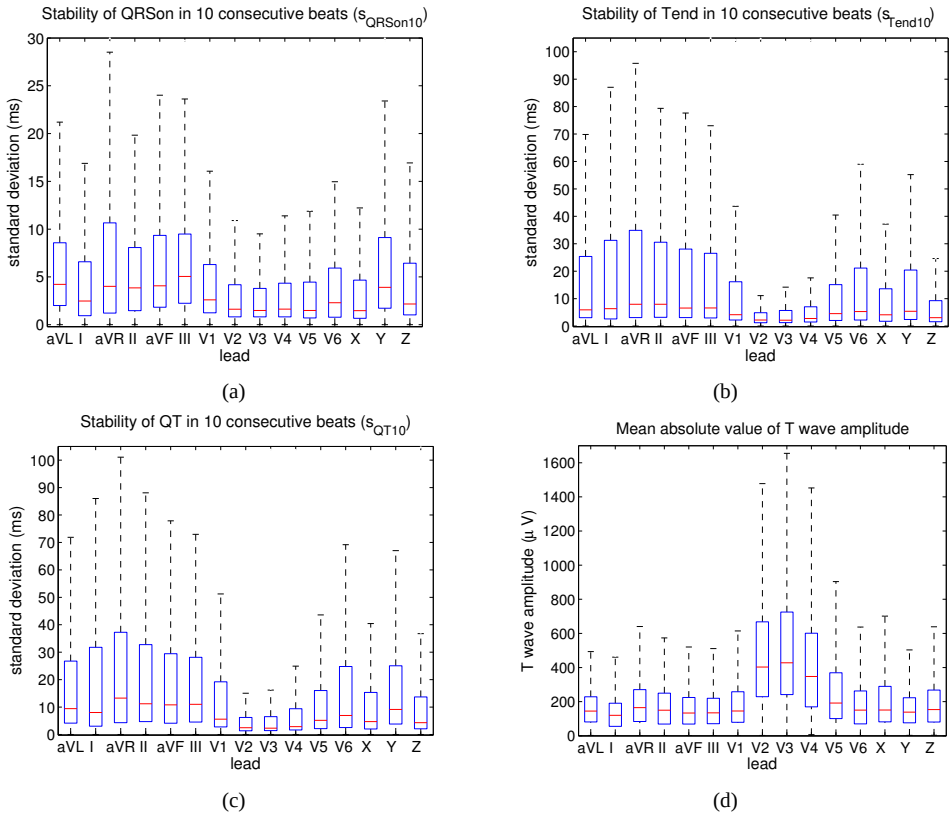

Figure 3. Box and whiskers plots of (a) $s_{QRSon10}$, (b) s_{Tend10} , (c) s_{QT10} and (d) T_{amp} in the available leads.

wave electrical axis. This results can be explained by the higher signal-to-noise ratio in those leads and their lower sensitivity to rotations in the heart electrical axis. These results emphasize the importance of lead selection when measuring the QT interval, and suggest that increased stability may be attained by measuring a global, multilead QT interval instead of single-lead measurement.

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