A Computationally Efficient Method to Quantify the Biometric Properties of Ventricular Repolarization Irregularities in Healthy and Diseased Human Subjects

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Abstract

Repolarization heterogeneity expressed by QT interval prolongation and abnormal temporal dynamics of the QT interval time series is an important factor in relation to coronary heart disease and lethal arrhythmias.

Based on our observations, the calculation of window correlation between the mean and variance of features extracted from QT interval time series can reveal natural and disease specific fluctuation patterns. Our algorithm is potentially a sensitive biometric measure to quantify personalized differences and the properties of repolarization heterogeneity, and also a potential biomarker to characterize disease specific QT interval temporal dynamics.

1. Introduction

Several statistical measures have been worked out to quantify different patterns that characterize the impaired and natural circadian control of repolarization properties based on QT interval features like SDQT and QTVi [1,2,3]. It has been proven by a variety of clinical studies that repolarization heterogeneity can prognosticate sudden cardiac death and arrhythmia [4,5,6].

Based on the above mentioned results it is still an open question if there exists an optimal or specific temporal window size to calculate SDQT and QTVi from long term QT interval time series under specific healthy or diseased conditions.

Another open question is the relation of mean and variance of different QT interval features extracted from different temporal windows under healthy and diseased conditions. Window correlation based methods investigating the relation between the mean and variance of QT interval time series have not been thoroughly investigated.

The primary goal of the study was to characterize the temporal dynamics of the above mentioned standard and newly developed features extracted from the QT interval time series.

The secondary goal of the study was to describe and quantify the window size (length of observation time) dependence of the features extracted from the QT interval time series among healthy and diseased populations.

2. Methods and Datasets

The QT database of PhysioNet was used to collect Lead I ECG recordings for the data analysis: https://physionet.org/physiobank/database/qtdb/doc/index.shtmlandhttps://physionet.org/physiobank/database/qtdb/doc/node4.html
Approximately 1000 heartbeat-long noise and artefact free ECGs were collected from three separate groups of the QT database:

- MIT-BIH Normal Sinus Rhythm Database (indexed by "h" in the followings)
- MIT-BIH Arrhythmia Database (indexed by "a" in the followings)
- sudden death patients from BIH (indexed by "s" in the followings).

Both from the "h", "a" and "s" groups only those ECGs were analyzed where the waveform pattern was classified as: (p) (N) t) u). Sample sizes were 10 (group "h"), 8 ("a" group) and 11 ("s" group). The QRS complex and the QT interval was determined by AcqKnowledge 5.0 software and the calculations described below were carried out in Matlab.

The following formulas were used to calculate the SDQT and QTVi values [3]:

$$\text{SDQT} = \frac{1}{N-1}\sum_{i=1}^{N}(QT_i - QT_{mean})^2$$

$$\text{QTVi} = log10\left(\frac{\frac{SDQT^2}{QT_{mean}{}^2}}{\frac{SDRR^2}{RR_{mean}{}^2}}\right)$$

The SDQT and QTVi values were computed for different number of heartbeats by moving window averaging along the QT interval time series. The different number of heart beats (number of QT intervals) was defined as the window size and was adjusted between i = (5:25). The step size for the moving average was always equal with 1. The mean and variance values for all the windows were computed in the case of the SDQT and QTVi moving averages.

The correlation between the mean and variance for a given window was expressed by the Pearson'

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correlation coefficient and afterwards indexed by Corr.SDQT and Corr.QTVi.

Grand averages presented on Fig.6 and 7. were calculated from all the subjects in each group to describe the window size dependence of a given feature extracted from QT interval time series.

3. Results

The natural fluctuation of the correlation between the mean and variance of the SDQT and QTVi moving average time series is visualized only in the case of the "h" group (Fig.1. and Fig.5.). Both in the case of the SDQT and QTVi time series a fluctuation was observed in the correlation coefficient values within the minute range.

The window size dependence of the SDQT and QTVi raw values and the correlation coefficients are compared and statistically analyzed in the case of the "h", "a" and "s" groups (Fig.6., Fig.7. and Table 1).

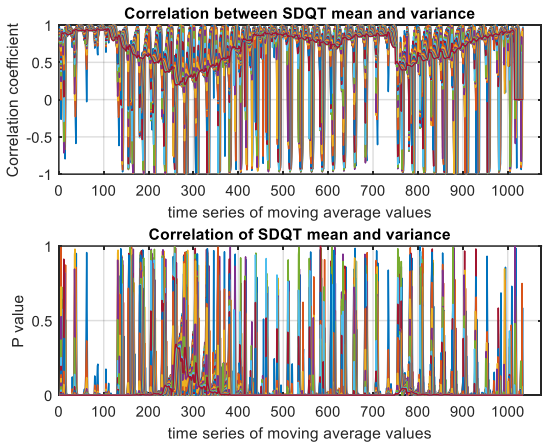


Figure 1. Correlation between the mean and variance of the SDQT moving average time series is shown for all the window sizes (5:25) and plotted by different colours. P values calculated by a moderated t-test are also shown in the bottom. Heart beats are represented on the x axes.

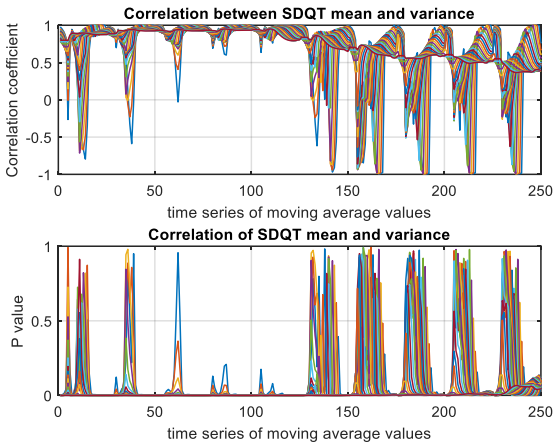


Figure 2. Correlation between the mean and variance of the SDQT moving average time series is shown for all the window sizes (5:25) and plotted by different colours. P values calculated by a moderated t-test are also shown in the bottom. The figure is magnified along the x axis comparing to fig.1.

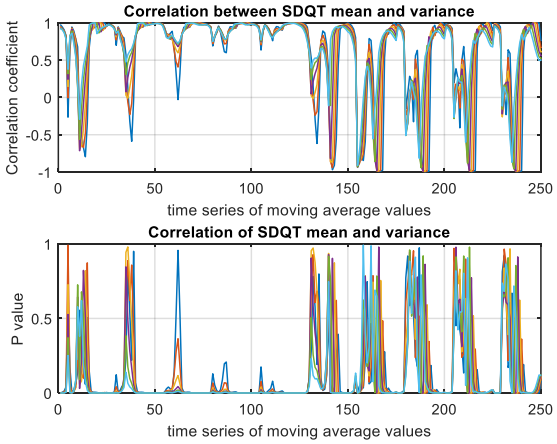


Figure 3. Correlation between the mean and variance of the SDQT moving average time series is shown for window sizes from 5 to 10 and plotted by different colours. P values calculated by a moderated t-test are also shown in the bottom. The figure is magnified along the x axis comparing to fig.1.

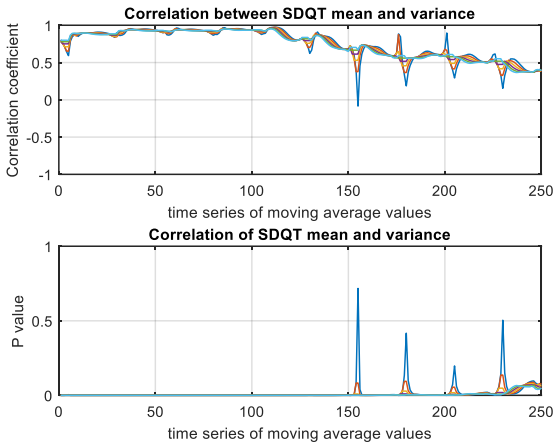
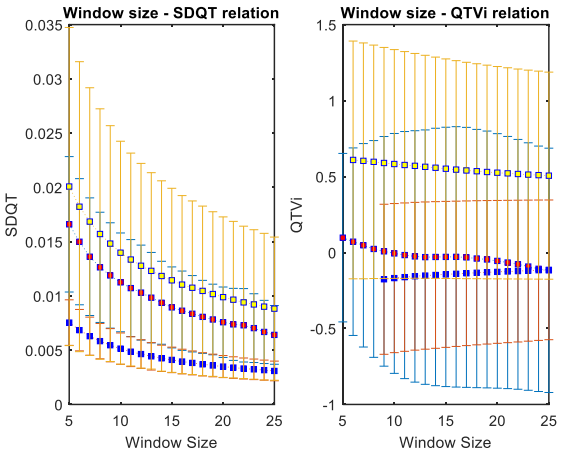


Figure 4. Correlation between the mean and variance of the SDQT moving average time series is shown for window sizes from 20 to 25 and plotted by different colours. P values calculated by a moderated t-test are also shown in the bottom. The figure is magnified along the x axis comparing to fig.1.



Figue 6. The mean and standard deviation values of the SDQT and QTVi moving window averages calculated for all the subjects in a given group are plotted against the different window sizes (5:25). Mean values are represented by different colours indicating the compared groups as follows: blue - “h”, red - “a”, yellow – “s”.

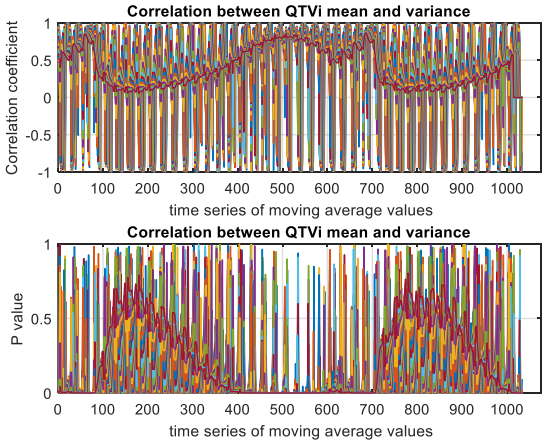
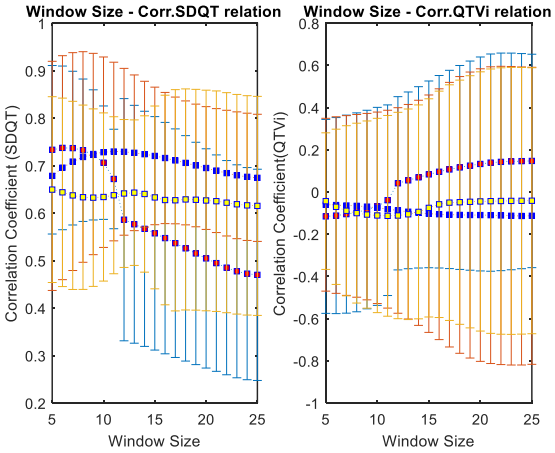


Figure 5. Correlation between the mean and variance of the QTVi moving average time series is shown for all the window sizes (5:25) and plotted by different colours. P values calculated by a moderated t-test are also shown in the bottom. Heart beats are represented on the x axes. (The magnified figures are not shown as in the case of SDQT moving averages due to the limited length of the article.)



Figue 7. The mean and standard deviation values of the correlation coefficients calculated from the SDQT and QTVi moving window means and variances are plotted against the different window sizes (5:25). Mean values are represented by different colours indicating the compared groups as follows: blue - “h”, red - “a”, yellow – “s”.

Win. Size	SDQT h-a	QTVi h-a	Corr SDQT h-a	Corr QTVi h-a	SDQT h-s	QTVi h-s	Corr SDQT h-s	Corr QTVi h-s
5	1	0	0	0	1	0	0	0
6	1	0	0	0	1	0	0	0
7	1	0	0	0	1	0	0	0
8	1	0	0	0	1	0	0	0
9	1	0	0	0	1	1	0	0
10	1	0	0	0	1	1	0	0
11	1	0	0	0	1	1	0	0
12	1	0	0	0	1	1	0	0
13	1	0	0	0	1	1	0	0
14	1	0	0	0	1	1	0	0

15	1	0	0	0	1	1	0	0
16	1	0	0	0	1	1	0	0
17	1	0	0	0	1	1	0	0
18	1	0	0	0	1	1	0	0
19	1	0	1	0	1	1	0	0
20	1	0	1	0	1	1	0	0
21	1	0	1	0	1	1	0	0
22	1	0	1	0	1	1	0	0
23	1	0	1	0	1	1	0	0
24	1	0	1	0	1	1	0	0
25	1	0	1	0	1	1	0	0

Table 1. Statistical difference between features extracted from QT interval time series was tested by two sample t-test. SDQT, QTVi, Corr.SDQT and Corr.QTVi values were compared between the healthy and diseased populations (h-a and h-s comparisons). Statistically significant difference was accepted at $p<0.05$ level and indexed by 1 in the table. Zeros are representing the $p>0.05$ values in a given comparison. Note the high sensitivity of the SDQT feature and the window size dependence of the Corr.SDQT feature in the "h-a" comparison.

4. Discussion

Three approaches were combined to map and describe the temporal microstructure of the QT interval dynamics:

- calculation of the SDQT and QTVi values for different window sizes by a moving average method,
- calculation of the window correlation between the mean and variance of the SDQT and QTVi moving averages and
- statistical comparison of the window size relation of the above mentioned features between healthy and diseased groups.

Both in the case of Corr.SDQT and Corr.QTVi time series a minute range fluctuating pattern of significant coupling and non-significant decoupling between the mean and variance was observed and shown on Fig.1-5.

Based on the results summarized on Fig.6-7. and table 1. we can conclude the following:

- moving average SDQT is a highly sensitive statistical measure in the case of all observed temporal window sizes to quantify the difference between healthy and diseased populations,
- moving average QTVi is a sensitive measure only in the case of longer temporal window sizes [9:25] to detect statistical difference between healthy and "sudden cardiac death" groups but insensitive to detect difference between the healthy and arrhythmia group,
- Corr.SDQT showed a specific window size dependence in the sensitivity of detecting statistical difference between the healthy and arrhythmia group while showed no sensitivity against the difference between the healthy and "sudden cardiac death" groups, and
- Corr.QTVi showed only a non-significant difference within the "h-a" comparison, generally was proven to be an insensitive measure to detect differences between the observed groups.

Despite the low sample size and the problems of cross-database comparisons, the approach of investigating the temporal window size dependence of QT interval dynamics is a promising tool to develop disease specific statistical measures.

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