Assessment of QT-RR intervals relation in patients with atrial fibrillation

L. Iozzia[1], L. T. Mainardi[1], F. Lombardi[2], V. D. A. Corino [1]

[1] Dipartimento di Elettronica, Informatica e Bioingegneria, Politecnico di Milano, via Golgi 32, 20133 Milan, Italy
[2] U.O.C. di Malattie Cardiovascolari, Fondazione IRCCS Ca Granda Ospedale Maggiore Policlinico, Dipartimento di Scienze Cliniche e di Comunitá, Universitá degli Studi di Milano, Milan, Italy

Abstract

QT-RR relation has been deeply investigated during sinus rhythm. However there are not established methods for the evaluation of QT-RR relation in patients with atrial fibrillation (AF). The aim of the present study was to assess the relation between QT and preceding RR intervals in ECG signal of patients with AF using different methods. We analysed data from 26 patients with persistent AF. A two-step procedure was used to detect T wave apex.

In order to consider QT lag phenomenon during AF, the relation between RT and RR intervals was assessed by different methods, using from 1 to 5 preceding RR intervals. A linear regression was applied to compare the slopes.

A slightly increase of the QT-RR slope was observed when a larger number of preceding RR intervals was considered ($RT - RR_1$ 0.030 ± 0.013, $RT - RR_{1-2}$ 0.028 ± 0.012, n.s., $RT - RR_{1-3}$ 0.033 ± 0.012, n.s., $RT - RR_{1-4}$ 0.035 ± 0.016, $p < 0.0001$, $RT - RR_{1-5}$ 0.039 ± 0.018, $p < 0.0001$, $RT - RR_{(1-5)m}$ 0.048 ± 0.022, $p < 0.0001$, $RT - RR_2$ 0.000 ± 0.007, $p < 0.0001$). The most significant variation was observed among the mean value of $RT - RR_1$ slope with the mean value of $RT - RR_{(1-5)m}$ slope. Interestingly the RT-RR correlation was completely lost when only the second previous RR interval was considered.

1.   Introduction

During sinus rhythm the relation between RR and QT intervals has been deeply studied [1, 2].

The relationship between QT and RR intervals was often simplified to a curvilinear relationship represented by Bazett [3] or Fridericia [4] QT correction formulae. Adjustment of QT to changing heart rate is a dynamic phenomenon called *QT lag*, consisting of fast and slow adaptation phase. Franz et al [5] showed that after rapid change in heart rate, fast adaptation phase of repolarization usually lasts from 30 to 60 seconds followed by a 2-minute slow adaptation.

The QT adjustment seems to be highly individual and dependent on the velocity of heart rate change.

During AF, QT variability reflects the severity of the underlying cardiac disease [6]. However, very few studies have focused on the relationship between QT and RR intervals in AF [6–8]. A previous study by Fujiki et al. [7] correlated the QT intervals to a weighted average of five RR intervals (mRR), showing that the slope of QT-mRR during AF became closer to that of QT-RR during sinus rhythm compared with that of QT-RR during AF.

The aim of this study was to assess the relation between QT and RR intervals in patients with AF using different methods.

2.   Methods

2.1.   Study protocol

We analysed 26 consecutive patients (64 ± 12 years, 16 males and 10 females) admitted to the hospital for programmed electrical cardioversion (EC) for persistent AF according to international guideline indication (i.e. an AF episode lasting longer than 7 days and requiring termination by EC). The mean duration of arrhythmia was 6 ± 1 months.

The study conforms to the Declaration of Helsinki, and was approved by the Ethics Committee of San Paolo Hospital in Milan (Italy). All patients gave their written informed consent for the procedures related to the study.

Surface electrocardiogram (ECG) was acquired for about 10 min before and 2 hours after EC, two leads were recorded with a Task Force Monitor (CNSystem) recording system. The sampling frequency was 1 kHz, raw data were exported as ASCII text files for offline analysis.

2.2.   Series extraction

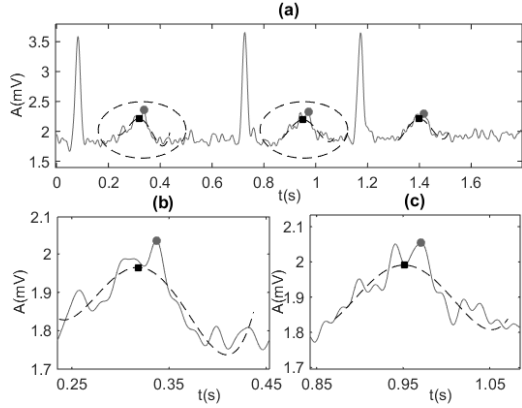*RR series*: An automatic QRS detection algorithm was used to locate R waves on the ECG and the RR inter-

Figure 1. (a) segment of ECG signal obtained from the modulation of the two leads acquired for one patient with the comparison between the coarse localization of T peak and the successive refinement signed by dashed line; (b), (c) zooming of two T waves. The gray dot is the first T peak localization, while black square is the T apex detected by the application of polynomial curve.
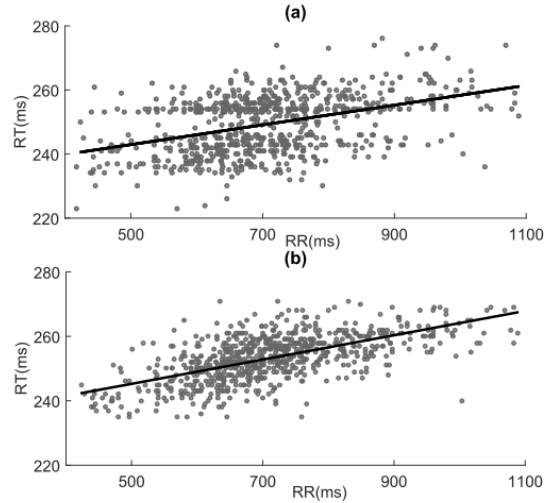

Figure 2. RT-RR scatter plot and regression line for one patient: (a) T peaks were identified as the highest value in the temporal window defined by two consecutive QRS complexes; (b) T peaks detection realised by the two step procedure.

vals measured as the distance between two consecutive R waves. Ventricular ectopic beats were excluded from the analysis. An interactive graphic interface allowed the operator to visually identify and correct missed QRS beats.

RT series: Repolarization duration was defined as the time interval between R apex and T apex (RT). The RT measurement avoids the problems of identification of both Q wave onset and T wave offset, associated to measurement of QT interval (particularly difficult to be detected during AF). The ECG signal was filtered by a third order pass-band Butterworth filter with cut-off frequencies $f_1 = 0.5Hz$ and $f_2 = 40Hz$. A constant offset ($c = 2$) was applied to the amplitude of both two leads signals and the averaged ECG was computed as the square root of the sum of the square of the two leads. A window w_1 between two consecutive QRS complexes of length equal to 80% of the RR interval was identified. Because of the presence of f-waves that affects ECG signal, the procedure to identify the T apex consists of two major steps: i) coarse localization of T apex; ii) refinement of T apex position. In step i) the apex of the T wave was defined as the local maximum in the window w_1 (they are labeled as T_i). In step ii),

the points T_i were taken as coarse temporal reference for each T apex, whose timing was then refined by fitting the T wave by a 4th polynomial curve. The T wave to be fitted was defined as the wave in the window $T_i \pm \Delta$, defined as w_2, where Δ was set to 100 ms. The final position of T apex was defined as the local maximum in the window w_2 of the polynomial curve. Figure 1 shows an example of identification of T peaks applying the polynomial fitting.

Finally a cross-correlation between each T wave and an a priori template was computed and waves with cross-correlation lower than 0.9 were excluded from the analysis.

In both RR and RT series, some outliers may be present and they have to be excluded. RR intervals were divided into 10 bins, and the bins located at the two tails of the histogram containing less than 1% of the total RR intervals were removed. RT intervals were defined as outliers if they fell outside the range defined as $mean(RT) \pm 3*mad$, where *mad* is the median absolute deviation.

2.3. RT-RR relation

The correlation between RT and RR intervals was computed applying seven different methods:

1) the i-th RT interval is correlated with the first previous (i-1)-th RR interval;
2) the i-th RT interval is correlated with the average of the two previous RR intervals, i.e. the (i-1)-th and the (i-2)-th intervals;

Table 1. ECG parameters characteristics.

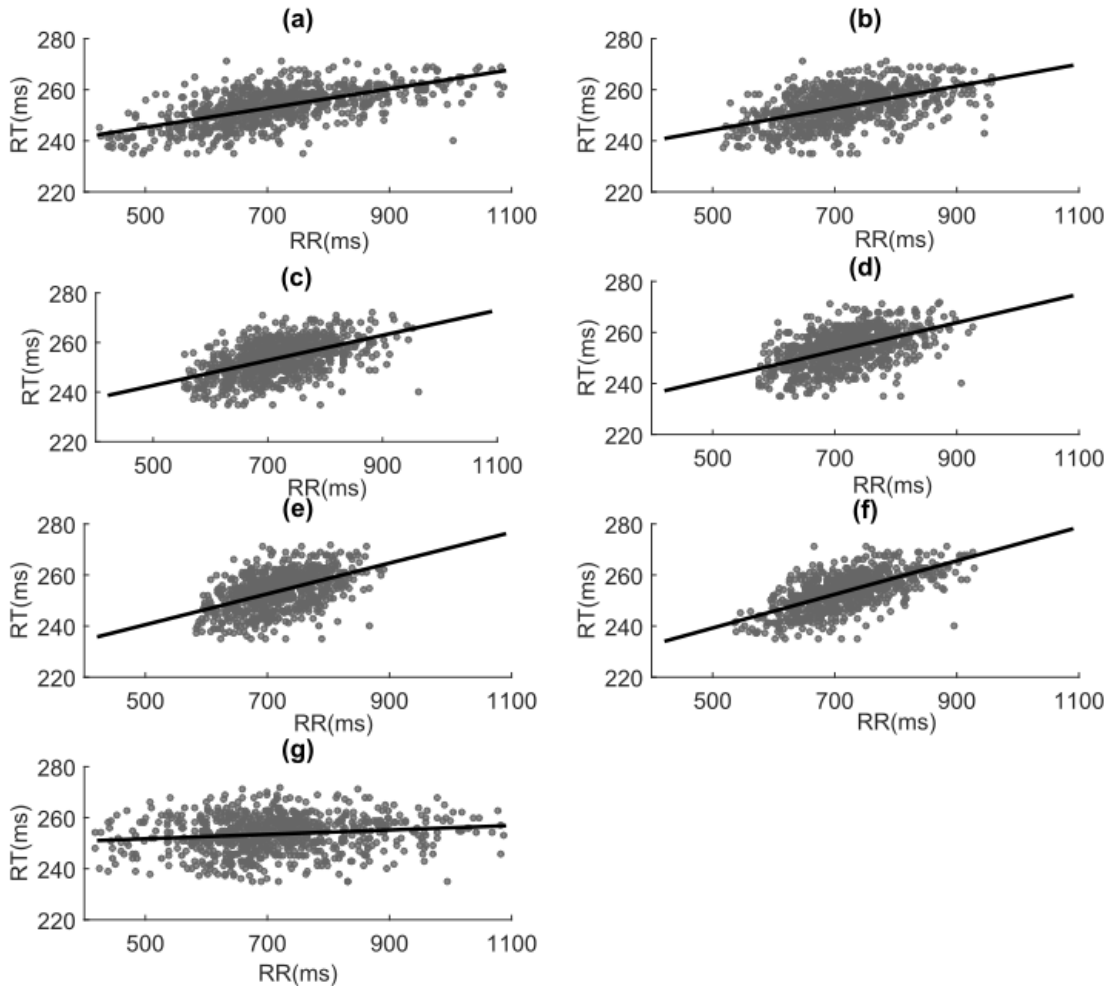| Parameter	Rest AF
$meanRR(ms)$	717 ± 149
$SDNN(ms)$	142 ± 45
$meanRT(ms)$	231 ± 20

Figure 3. RT-RR scatter plot and regression lines for one patient for seven different methods: (a) first method; (b) second method; (c) third method; (d) fourth method; (e) fifth method; (f) sixth method; (g) seventh method.

3) the i-th RT interval is correlated with the average of the three previous RR intervals, i.e. the (i-1)-th, the (i-2)-th and (i-3)-th intervals;

4) the i-th RT interval is correlated with the average of the four previous RR intervals, i.e. the (i-1)-th, (i-2)-th, (i-3)-th and (i-4)-th intervals;

5) the i-th RT interval is correlated with the average of the five previous RR intervals, i.e. the (i-1)-th, (i-2)-th (i-3)-th, (i-4)-th and (i-5)-th intervals;

6) the i-th RT interval is correlated with a weighted average of previous five RR intervals: $RR = (0.5 * RR_{i-1} + 0.2 * RR_{i-2} + 0.1 * RR_{i-3} + 0.1 RR_{i-4} + 0.1 * RR_{i-5})$. This method gives the highest weight to RR interval immediately preceding the RT and a decreasing weight to previous RR intervals;

7) the i-th RT interval is correlated with the second previous RR interval, i.e., the (i-2)-th interval.

The first method is the most commonly used to analyse the correlation between RT and RR intervals and the sixth one was introduced in [9] for recordings during AF. For each method a robust linear regression was performed to study the relation between RT and RR intervals.

2.4. Statistical analysis

The results are given as mean and one standard deviation. A one-sided paired t-test was used to compare different methods applied to rest phases during AF. A value of $p < 0.05$ was considered significant.

Table 1 shows the mean of RR and RT intervals during AF, and SDNN is the standard deviation of all RR intervals.

3.   Results

The detection of T peaks as the highest value found in the interval between two QRS complexes determines a RT-RR scatter plot divided into two clusters, as it can be seen in Figure 2-a. In fact, the presence of superimposed atrial fibrillatory wave add several local maxima in the signal, which mask the true location of the apex of the T wave. The application of two step procedure in T peaks detection bypasses this problem and generate a less-scattered RT-RR plot (see Figure 2-b).

Figure 3-a shows an example of the RT-RR scatter plot for one patient, when the first method is adopted, with the corresponding regression line. In Table 2 the average slope is represented for the whole population as obtained for the different methods. A significant increase in the average slope, when compared to the first method, is observed in method 4, 5 and 6. The highest increase is evident when the comparison is made between the first and the sixth method. On the contrary the RT-RR relationship is completely lost when RT interval is correlated with the second previous RR interval (method 7).

Table 2.   Slopes of regression lines between RT and RR intervals during rest phase in AF; $*: p < 0.001$, $**: p < 0.0001$.

Slope	Rest AF
$Slope_1$	0.030 ± 0.013
$Slope_2$	0.028 ± 0.012
$Slope_3$	0.033 ± 0.012
$Slope_4$	$0.035 \pm 0.016^*$
$Slope_5$	$0.039 \pm 0.018^{**}$
$Slope_6$	$0.048 \pm 0.022^{**}$
$Slope_7$	$0.000 \pm 0.007^{**}$

In Figure 3 a graphical comparison among all methods is made considering one patient. As it was shown previously, by relating the RT interval with an increasing number of preceding RR intervals, the slope of regression line increases.

3.1.   Discussions

To our best knowledge, there are few studies that have deepened the QT-RR relationship during AF.

We decided to focus our attention on the influence that preceding RR intervals have on the RT interval, and how this influence could be taken into account in analysis step.

The most significant result was the constant increase of the slope of the regression line, when more preceding RR intervals were considered. The following result is concordant with preceding studies [6–8], where, applying the

sixth method, the slope increased significantly compared to the slope obtained by the first method.

Moreover the RT interval seems to be greatly influenced by the first preceding RR interval. Indeed the seventh method showed the lost of RT-RR relationship when only the second previous RR interval was correlated to RT interval.

The reasons behind this phenomena need to be clarified in future works. This could be related to the adopted methodologies or could be the evidence of some physiological behavior which deserves to be exploited.

Finally, we believe that the detection of RT interval is more robust compared to the detection of QT interval. Indeed in AF the presence of f-waves affects the ECG signal, so the identification of Q onset and T offset is difficult to achieve.

References

[1] Qiu H, Bird GL, Qu L, Vetter V, White P. Evaluation of QT interval correction methods in normal pediatric resting ECGs. CinC 2007;34:431–434.

[2] Malik M, Fräbom P, Batchvarov V, Hnatkova K, Camm AJ. Relation between QT and RR intervals is highly individual among healthy subjects: implications for heart rate correction of the QT interval. Heart 2002;87:220–228.

[3] Bazett H. An analysis of the time relations of electrocardiograms. Heart 1920;53–503.

[4] Fridericia L. Duration of systole in electrocardiogram. Acta Med Scan 1920;53–469.

[5] Franz M, Swerdlow C, Liem L, Schaefer J. Cycle length dependence of human action potential in vivo. effects of single extrastimuli sudden sustained rate acceleration and deceleration, and different steady state frequencies. J Clin Invest 1988;82:972–979.

[6] Larroude CE, Jensen BT, Agner E, Toft E, Torp-Pedersen C, Wachtell K, K. KJ. Beat-to-beat QT dynamics in paroxysmal atrial fibrillation. Heart Rhythm Society 2006;3:660–664.

[7] Fujiki A, Yoshioka R, Sakabe M, Kusuzaki S. QT/RR relation during atrial fibrillation based on single beat analysis in 24-h Holter ECG: the role of the second and further preceding RR intervals in QT modification. J Cardiol 2011;57:269–274.

[8] Darbar D, Hardin B, Harris P, Roden DM. A rate-independent method of assessing QT-RR slope following conversion of atrial fibrillation. Journal Cardiovasc Electrophysiol 2007;18:636–641.

[9] Ehlert FA, Goldberg JJ, Rosenthal JE, Kadish AH. Relation between QT and RR intervals during exercise testing in atrial fibrillation. Am J Cardiol 1992;70:332–338.

Address for correspondence:

Luca Iozzia

Dipartimento di Elettronica, Informatica e Bioingegneria, Politecnico di Milano, via Golgi 32, 20133 Milan, Italy
luca.iozzia@polimi.it