Automated QT/RR Analysis Based on Selective Beat Averaging Applied to Electrocardiographic Holter 24 H

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Abstract

The study of QT/RR relationship is important for the clinical evaluation of possible risk of acquired or congenital ventricular tachyarrhythmias, predisposing to life-threatening arrhythmias. To improve the signal-to-noise ratio and obtain automated and reliable QT measurements from Holter ECG 24 h, a new approach based on selective beats averaging was applied. A total of 102 healthy subjects (range 30-75 years, 53 women, 52.8 ± 11.0 years, and 49 men, 56.6 ± 11.8 years) were studied to obtain QT/RR normality curves (±2SD around mean value) separately for day and night-time. Gender-related and circadian differences in the QT/RR relation were noticed, showing the potential utility and application of this analysis to derive physiological observations on repolarization mechanisms.

1. Introduction

Since the advent of electrocardiography, the study of the relation between the ventricular repolarization duration (QT interval) and the cardiac cycle duration (RR) has represented an important field of research, together with the evaluation of which formula could have been able to represent it. From a physiologic point of view, the QT duration represents the interval from the earliest activation to the latest repolarization of ventricular myocardium cells. Changes in its relationship with the RR duration have been indicated as index of risk of acquired or congenital ventricular tachyarrhythmias that can predispose to life-threatening arrhythmias [1].

In clinical practice, the QT analysis is based on the manual measurement of RR and QT duration on a few ECG beats, on the application of a correction formula [2], and on the comparison of the QT corrected value with the clinically defined normality range. In the last decade, new analysis tools have been implemented in the ECG Holter 24 h analysis equipments, in the attempt to provide reliable and automatically obtained indices of QT/RR relation, able to discriminate between normality and pathology [3]. The major limitation of these methods relies on the fact that, to automatically obtain the QT and RR duration measurements from a 200 Hz sampled signal, characterized by a low signal-to-noise ratio (SNR) as is the ECG Holter, an average operation by a moving non-overlapping 30 second temporal window has to be performed. In this way, beats of different duration are averaged together, thus obtaining a template with improved signal-to-noise ratio, but with altered T wave morphology.

To overcome this limitation, the aim of this study will be to develop an alternative procedure for QT/RR analysis on ECG Holter signals, based on selective beat averaging [4], to reliably detect on the ECG the fiducial points needed for automated QT analysis but without averaging beats with different RR duration. This method will be applied to a population of 102 normal subjects, in order to define the normality ranges of the extracted parameters.

2. Methods

2.1. Population and material

From all the patients referred to an ECG Holter 24h examination at Niguarda Hospital in Milan in the last six months, we selected for the analysis 53 females (F) (mean±SD, 52.8 ± 11.0 years) and 49 males (M) (56.6 ± 11.8 years), diagnosed as normal on the basis of a clinical cardiologic work-up and not assuming any antiarrythmic drug.

During their examinations, a 3-lead ECG Holter 24 h was digitally acquired at 200 Hz and stored on a Flash Memory Card (PCMCIA standard) by a Syneflash Holter system (ELA Medical, Paris, France). SynetTEC software (ELA Medical, Paris, France) was then applied for conventional clinical analysis, thus obtaining R-wave detection (RR series), epoch of each event in the 24 hours and beats classification as output.

2.2. Selective beat averaging procedure

The ECG Holter 24h first standard lead, usually characterized by a major amplitude of the T wave, has been considered for the analysis, together with the

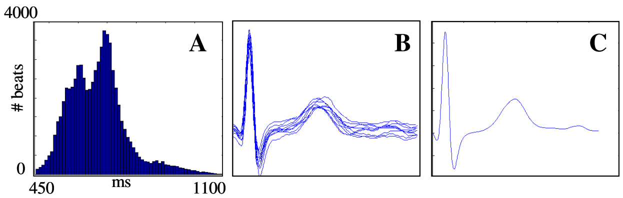

Figure 1. Example of the applied analysis method: the histogram of the 24h RR serie is computed (A); for each 10 msec bin, the corresponding beats were extracted from the ECG signal, oversampled and aligned in correspondence of the R wave (B). The result of the simple averaging operation is shown in C.

relevant RR serie and beats classification obtained by the SyneTEC software. Only the RR values which were classified as in sinusal rhythm, with an heart rate less than 133 bpm, and with a RR(i) > 75 % *RR(i-1), were included in the following analysis, thus excluding premature and extra-sinusal beats. First, the RR intervals were classified as day-time (from 8:00 to 21:00) and night-time (from 23:00 to 06:00), to apply the next steps to the analysis of day and night periods, separately.

A RR duration histogram with 10 msec bin amplitude was then computed, thus generating RR duration classes C (from 450 to 1450 msec, 10 msec step), each including beats which differ by a maximum of 2 samples. For each class C(n), the beats with the corresponding RR duration were located on the ECG signal, extracted and oversampled (from 200 Hz to 1000 Hz). After beats realignment according to the R wave peak [4], a simple averaging operation was then applied, thus obtaining a mean template T(n), representative of all the beats owing to the class C(n) (Figure 1).

2.3. Fiducial points detection and normality curves computation

For each template T(n) obtained from at least 30 beats, the isoelectric baseline was defined as the straight line connecting the first and the last point of T(n), and subtracted from it. Then, a procedure for the automated detection of some fiducial points, such as Tapex (defined as the maximum of T wave), Tend (defined as the intersection of the downward slope with the zero value), Tstart (defined as the intersection of the upward slope with the zero level) has been applied (Figure 2) [4-5].

Basing on these points, the following clinical parameters have been defined and computed: RT_{apex} and RT_{end} interval durations, T wave upward duration (early repolarization, T_{start}-T_{apex},) and T wave downward duration (late repolarization, T_{apex}-T_{end}), T wave amplitude maximum, T wave upward area (area underlying T_{start}-T_{apex}), T wave downward area (area

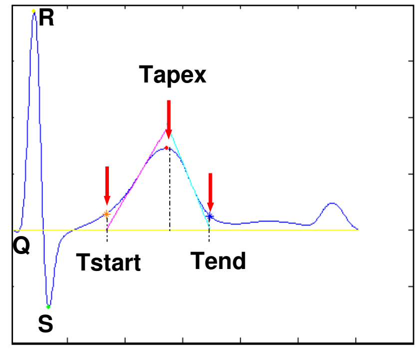

Figure 2. Fiducial point detection on the template T(n). Tstart and Tend were defined as the intersection of the upward and downward slope, respectively, with the zero level (after isoelectric line subtraction). Tapex was defined as the maximum of the T wave.

underlying T_{apex}-T_{end}). Moreover, the indices of temporal or amplitude symmetry were computed as the ratio between T wave upward and downward duration or amplitude, respectively.

For each subject, the curves representing the relation between the RR duration and each of the computed parameters were computed, both for day- and night-time.

Once analyzed all the subjects, normality curves relevant to each clinical parameter, separately for M and F, day- and night-time, were computed: the mean value of the parameter $\bar{p}(n)$ for each RR duration class C(n) was computed as the mean of the values obtained from each subject, weighted by the corresponding number of beats w(n) whose generated the template T(n):

$$\bar{p}(n) = \frac{\sum_{1}^{X} {}_i p_i(n) * w_i(n)}{\sum_{1}^{X} {}_i w_i(n)} \qquad (1)$$

where X=53 for F and X=49 for M. To define a normality range of ±2SD (95% confidence interval) around the mean value, the corresponding SD was computed as:

$$\sigma_p(n) = \sqrt{\frac{\sum_{1}^{X} {}_i (\bar{p}(n) - p_i(n))^2 * w_i(T)}{\sum_{1}^{X} {}_i w_i(T) * (X-1)}} \qquad (2)$$

3. Results

In total, we analyzed 8.838.600 heart cycles, subdivided as follows: 6.142.696 during the day (2.749.170 for M and 3.393.526 for F); 2.695.904 during the night (1.234.719 for M and 1.461.185 for F). A mean of 1.090 beats were included in the computation of each

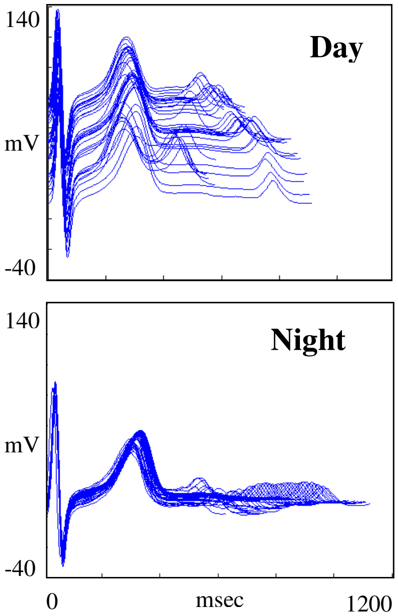

Figure 3. Example of all the templates relevant to all the classes of RR duration computed from a male subject. An augmented dispersion both in amplitude and duration of the computed templates is noticeable in this subject.

template (range 30 - 4174 beats). The selective beat averaging procedure appeared able to highly improve the SNR, resulting in templates on which the automated fiducial point detection was feasible and reliable.

In Figure 3 an example of the templates obtained in a male subject is shown: it is possible to appreciate the greater dispersion both in amplitude and in duration of the templates during the day, compared with those relevant to the night. In Figure 4, the relationship found between RT_{apex} and RT_{end} durations with RR is shown, separately for day and night, and M and F. Despite the existence of intersubject differences in QT relation [6-7], the values of the RT duration parameters showed a reduced standard deviation around their mean values, except for longer RR, where the dispersion was higher. During the day, it was worth note as the F had a range of RR values reduced compared to M. Moreover, the initial slopes of both relations for short RR (<600msec) were significantly different between M and F, in particular during the day (RT_{apex} : 0.19 for F and 0.33 for M; RT_{end}: 0.30 for F, 0.41 for M). A substantial linear dependence of RT_{apex} and RT_{end} duration on RR (>600msec) has been evidenced, with a lengthening of both parameters at the same RR during the night, particularly about women, characterized by lower SD than men's one.

Figure 5 shows the relations in M and F relevant to the day period between the durations of the first (T_{start} $-T_{apex}$) and the second (T_{apex}-T_{end}) part of the T wave with the RR. Interestingly, in M the late repolarization duration appeared not to be related with RR, while in F the dependence was visible only for RR<600msec; on the contrary, early repolarization duration seemed to have a monoexponential relation with RR, both in M and F. This reveals a T wave asymmetrical morphology, with a T wave upward slope area and duration that were always greater than T wave downward slope ones, except for high heart rates (RR<600 msec) during the day. Both the temporal and amplitude symmetry indices reflected this behaviour, which was maintained also during the night.T wave upward and downward areas, not visualized for lack of space, showed a monoexponential relation with RR duration in M, both during the day and night, and in F during the day, with a prevalence of T wave upward area, except for RR<600 msec where the amplitude ratio was <1. On the contrary, in F during the night both T wave upward and downward areas showed a parabolic relation with RR duration, with the maximum around RR=900 msec.

4. Discussion and conclusions

Automated analysis of QT interval from Holter recordings represents a difficult task. The proposed procedure of selected beat averaging appeared able to overcome some of the limitations connected with previous averaging methods, revealing to be effective in

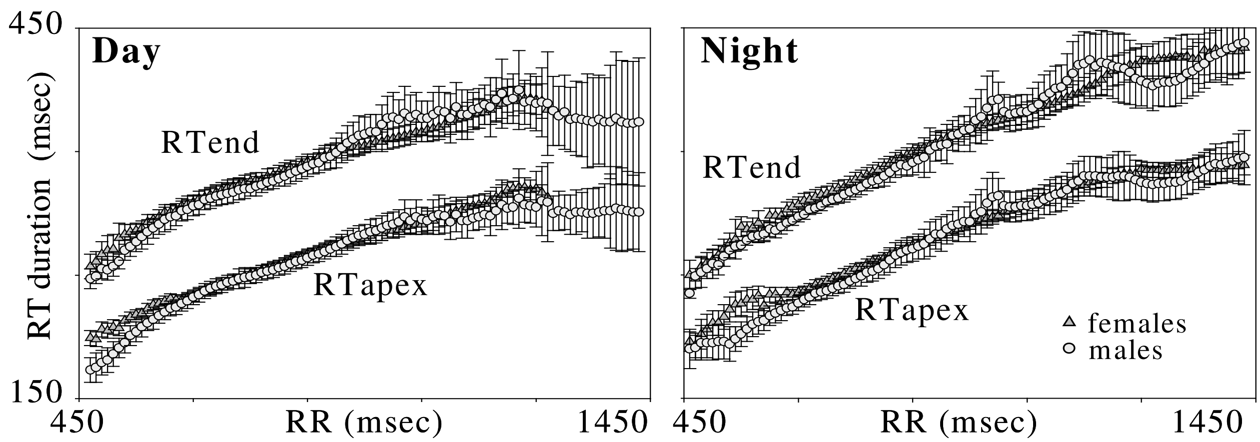

Figure 4. Normal ranges (mean± 2SD) of QT/RR relationship, relevant to RTapex and RTend duration, obtained in 49 males and 53 females, separately for day- and night-time.

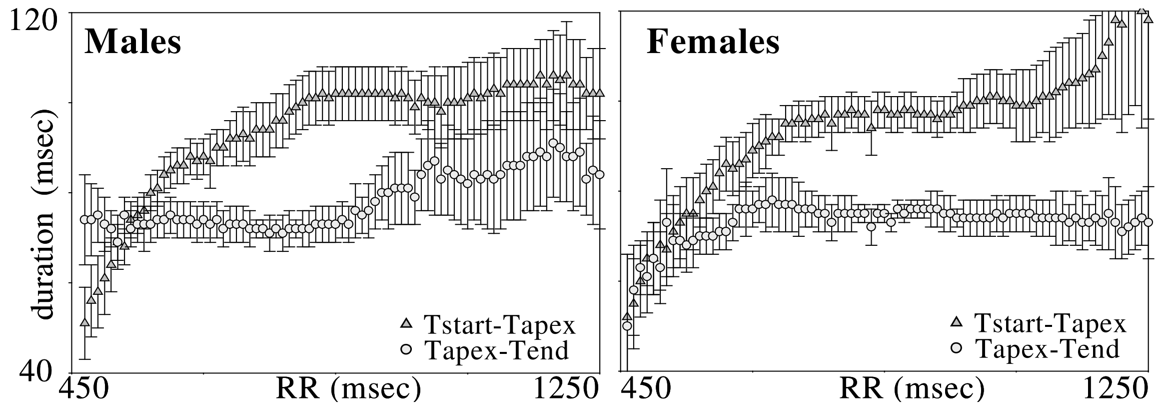

Figure 5. Normal ranges (mean±2SD) of QT/RR relationship, relevant to early (Tstart-Tapex) and late (Tapex-Tend) repolarization, obtained in 49 males (left) and 53 females (right), relevant to the day-time.

the improvement of the SNR, due to the high number of beats included in each of the 10 msec duration classes, while not affecting the T wave original morphology. This allowed the automatic detection of fiducial points (T wave start, apex and end) for the calculation of repolarization parameters from each template to be fast and reliable. The observed dispersion in amplitude in the templates obtained from healthy subjects during the day and their uniformity during the night are in agreement with data reported in literature [8]. The relationship between repolarization parameters and RR duration was then visualized in a rapid and immediate way in each subject. For each parameter, the computation of global curves based on weighted mean allowed the different distribution of RR durations for each subject to be taken into account in the determination of normality ranges. Different behaviours in the QT/RR relation were noticed both between M and F, and day and night, showing the potential utility and application of this kind of analysis to derive physio-pathological observations, when compared with curves obtained from patients with abnormal T wave. In particular, substantial linear dependence of RT_{apex} and RT_{end} duration with RR was found, characterized by a greater slope for RR<600 msec during day-time, especially in M. Again for RR<600 msec, a strong linear relation between early repolarization and RR duration was observed both in M and F during the day. The increased initial slope could be related to the higher sympathetic modulation existing at high heart rates, which influences the QT/RR relationship. Interestingly, no dependence was observed in late repolarization in M for RR<600 msec, which could be related to a gender different transmural dispersion of ventricular repolarization [9].

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