Beat-to-beat *T*-peak *T*-end Interval Duration Variability Assessed by *RR*-Interval Histogram Analysis in Health Sedentary and Athlete

Olivassé Nasario-Junior[1], Paulo R. Benchimol-Barbosa[1,2], Jurandir Nadal[1]

[1]Programa de Engenharia Biomédica, COPPE, Universidade Federal do Rio de Janeiro, RJ, Brasil
[2]Hospital Universitário Pedro Ernesto, Universidade do Estado do Rio de Janeiro, RJ, Brasil

Abstract

Ventricular repolarization duration (VRD) to RR-interval coupling relates to autonomic control and myocardial electrical stability. T-peak to T-end (TpTe) interval defined as the interval between the peak and the end of the T wave is an index of transmural dispersion of repolarization (TDR) with potential clinical implication. However, the dynamic coupling between TpTe- and RR-interval still needs clarification. This study investigated TpTe- and RR-interval coupling to assess dynamic repolarization adaptation in healthy sedentary (Control; n = 10) and well-conditioned male subjects (Athlete; n = 10). Both groups underwent 15 min resting ECG. Supervised fiducial point detection was carried out after low-pass filtering at 15 Hz. Histogram of RR-interval series was calculated, with 100 ms class width, ranging from 600 ms to 1200 ms. For each class, mean of normal RR-intervals (MRR) and mean of the TpTe-interval (MTpTe) were calculated. Regression lines of MTpTe as function of MRR were computed and Student t-test compared slopes between groups ($\alpha < 0.05$). In Control and Athlete, respectively, MTpTe was 82.2 ± 6.2 ms and 94.4 ± 6.9 ms ($p < 0.05$) and MRR interval was 849.2 ± 109.1 ms and 1027.5 ± 124.0 ms ($p < 0.05$). MTpTe significantly increased as a function of MRR in Athlete, whereas, in Control, slope was nonsignificantly negative. In athletes, TpTe-interval increases as a linear function of RR-interval in a wide physiological RR-interval range at rest, whereas, in sedentary subjects, TpTe-interval remained unchanged.

1. Introduction

Regular aerobic exercise provides beneficial changes on the cardiovascular system, characterized by mechanical, autonomic and electrophysiological remodelling [1]. Autonomic remodelling is evidenced by both resting heart rate (HR) reduction and cardiac vagal modulation increase. On its turn, dynamic ventricular repolarization duration (VRD) to *RR*-interval coupling relates to myocardial electrical stability [2, 3, 4].

The relationship between VRD and cardiac cycle length may be employed as a risk marker of susceptibility to arrhythmias [5]. As it is already known, the *QT*-interval adapts to HR changes, which makes it difficult to compare the recorded *QT*-interval at different HRs. To allow such a comparison, the concept of corrected *QT*-interval (*QTc*) for HR has been developed and, additionally, several different formulas have been proposed to describe this compensation. Bazett's formula is the most used and, consequently, the most criticized [6]. It has also been shown that intervals including the *J*-point and the *T* wave peak carry most of the dependence of VRD on cardiac cycle length.

The interval between the peak and the end of the *T* wave (*TpTe*-interval) has been shown to provide an ECG approximation of transmural dispersion of repolarization (TDR) [7]. Thus, prolongation of this interval has been associated to an effective risk marker of ventricular arrhythmogenesis [8]. As part of the VRD, *TpTe*-interval is expected to carry intrinsic cardiac cycle length dependence. However, as *TpTe*-interval is the terminal part of VRD, representing the action potential phase three gradient across ventricular wall, its heart rate dependence is still controversial in a range of *RR*-intervals.

Previous studies replicated the dependence of VRD (by alternative *RT*-interval) on the cardiac cycle duration, indicating that the separation of VRD by *RR*-interval classes may be useful to compare different populations, by pairing common bands and dispensing HR correction [2, 3, 4]. The aim of the study was to present an analysis tool based on *RR*-interval histogram to assess dynamic relation between *TpTe*-interval and *RR*-interval duration. This tool was applied to assess both *RT*- and *TpTe*-interval to *RR*-interval dependence in athletes and healthy sedentary subjects.

2. Materials and Methods

2.1. Study population

Study population has already been described [3], and it was composed by Athletes (n = 10) and healthy sedentary

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subjects (n = 10). Sample data is summarized in Table 1.

Table 1: Anthropometric and demographic characteristics (mean ± SD) of the subjects who participated in the study

	Control	Athlete
Age (years)	29.0 ± 5.4	24.4 ± 7.2
BMI (Kg/m^2)	23.8 ± 3.8	20.7 ± 1.9
BSA (m^2)	1.8 ± 0.2	1.8 ± 0.2
APTD (cm)	21.3 ± 1.9	21.1 ± 1.2
LLTD (cm)	28.1 ± 3.2	28.0 ± 1.2
METs	8.7 ± 1.9	19.6 ± 1.3 *

BMI = body mass index; BSA = body surface area; APTD = anteroposterior thoracic diameter; LLTD = laterolateral thoracic diameter; METs = metabolic equivalents. * p = 0.001.

2.2. Signal acquisition, processing and wave detection

Signal acquisition and pre-processing protocols have been described previously [3, 9, 10]

The distance between the top of the *QRS* complex (*R* wave peak) and the peak of the *T* wave in normal beats defined *RT*-interval (Figure 1), which was employed in a sole purpose of analysing VRD adaptation over instantaneous cardiac cycle [2]. On the other hand, *TpTe*-interval comprehended the distance between the 'peak' and the 'end' of the *T* wave (Figure 1), being employed in analysing adaptation of TDR over instantaneous cardiac cycle. The *RR*-, *RT*-, and *TpTe*-intervals were analysed on *X* lead.

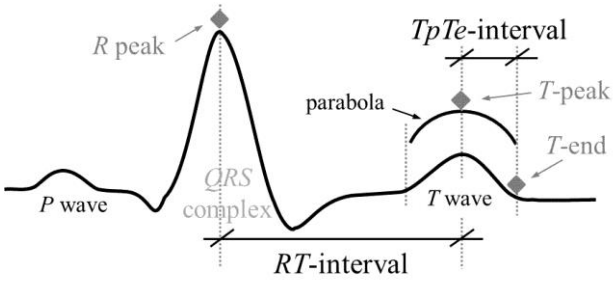

Figure 1. Identification of the 'peak' and the 'end' (fiducial points - ♦) on *R* and *T* waves, which allowed precise identification of the ventricular repolarization duration (VRD) and transmural dispersion of repolarization (TDR), represented by *RT*- and *TpTe*-intervals, respectively.

Fiducial points related to *T*-end were detected by employing an adapted method based on the trapezium's area approach [11]. A parabola function approach was fit to a segment limited by the onset and the offset of the respective *T* wave to find its peak (parabola vertex. See details in figure 1) [2]. Artefacts and ectopic beats were excluded by coefficient correlation (r) comparison between a reference beat template. Segments around T-peak and *T*-end fiducial points were extracted and employed to compare equivalent segments in each beat, where the r value threshold for segment acceptance or exclusion was defined after visual inspection carried out by one expert. Overall, fiducial points around segments in each detected beat that did not match the respective template segment were excluded from analysis. The percentage of beats discarded (mean ± SD) was calculated.

2.3. Dynamic *RR*-, *RT*- and *TpTe*-interval analysis

The histogram was constructed for each individual *RR*-interval series, and divided into classes of 100 ms width, ranging from 600 ms to 1200 ms, which represented a variation between 50 and 100 bpm in HR. For each histogram class, and respective to each *RR*-interval series, it was calculated mean (*MRR*) and standard deviation (*SDRR*) of consecutive normal *RR*-intervals; mean (*MRT*) and SD (*SDRT*) of consecutive normal *RT*-intervals; mean (*MTpTe*) and SD (*SDTpTe*) of consecutive normal *TpTe*-intervals. Only pairs of consecutive normal *RR*, *RT* and *TpTe*-intervals for individual series that lied inside a particular class of the *RR* histogram were analysed together.

For a particular histogram class (*class*) of the i^{th} subject, containing $N_{i,\,class}$ *RR*-intervals, the calculus of the mean ($Mx_{i,\,class}$), standard deviation ($SD_{xi,\,class}$) of the normal *RR*-, *RT*- and *TpTe*-intervals was performed as follows:

$$Mx_{i,class} = \sum_{k=1}^{N_{i,class}} \frac{x_K}{N_{i,class}} \quad (1)$$

$$SDx_{i,class} = \sqrt{\sum_{k=1}^{N_{i,class}} \frac{(x_K - Mx_{i,class})^2}{N_{i,class} - 1}} \quad (2)$$

where x represents either *RR*-, *RT*- or *TpTe*-interval.

For each histogram, classes with 20 or less intervals were excluded of analysis to avoid bias due to lack of statistical precision.

The values of the variables $Mx_{i,\mathrm{class}}$ and $SDx_{i,class}$ were aggregated to the respective histogram class. The pooled mean (Mx_{class}) and standard deviation (SDx_{class}) of *RR*-, *RT*-, and *TpTe*-intervals for each histogram class, weighted by respective degree-of-freedom ($\eta_{i,\,class}$), were calculated according to:

$$Mx_{class} = \frac{\sum_{i=1}^{20} Mx_{i,class} \cdot (\eta_{i,class} + 1)}{\sum_{i=1}^{20} (\eta_{i,class} + 1)} \quad (3)$$

$$SDx_{class} = \sqrt{\frac{\sum_{i=1}^{20}(SDx_{i,class})^2 \cdot \eta_{i,class}}{\sum_{i=1}^{20}\eta_{i,class}}} \quad (4)$$

where *x* represents either *RR*-, *RT*- or *TpTe*-interval.

The variables *MRT* and *MTpTe* were plotted and correlated with *MRR* class.

2.4. Statistical analysis

The *MRT*, *MTpTe* and *MRR* of each subject were pooled and averaged on a class-by-class basis in the control and athlete groups. Regression lines as function of *MRR* and, respective slopes (*sMRT and sMTpTe*) were computed for each group. Correlation coefficients (*r*) were tested before analysis, and Student t-test was used to compare slope between groups ($\alpha < 0.05$).

3. Results

The pooled *RR*-, *RT*- and *TpTe*-intervals duration, *MRR*, *MRT* and *MTpTe* respectively, were presented for each group in Table 2.

Linear correlation coefficient (*r*) and respective angular coefficient (*slope*) of regression lines between *MRR* and *MTpTe* variables are presented in Figure 2a. The *sMTpTe* values showed significant difference between groups ($p < 0.05$). *MTpTe* significantly increased as a function of *MRR* in athletes, whereas in sedentary control group slope was nonsignificantly negative.

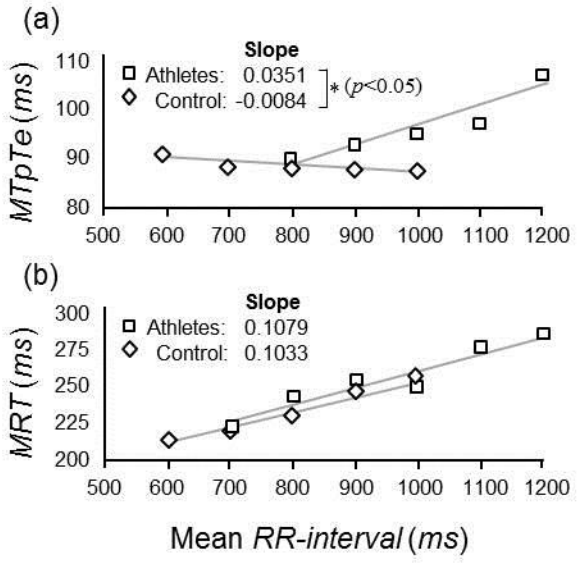

Figure 2. Pooled (a) mean *TpTe*-intervals (*MTpTe*) group analyses (Control and Athletes), and (b) mean *RT*-intervals (*MRT*) as a function of mean *RR*-intervals. Intergroup slope comparison (*$p < 0.05$).

The *r* and *slope* of regression lines between *MRR* and *MRT* variables are presented in Figure 2b. The s*MRT* values did not show significant difference between groups (p = NS). *MRT* significantly increased as a function of MRR in both groups ($p < 0.05$).

The percentage (mean ± SD) of discarded beats by $r \sim 0.99$ threshold, comparison to the template, was 27.1 ± 9.0 for the control group and 51.4 ± 16.7 for the athletes.

Table 2. *MRR*, *MRT* and *MTpTe* duration per group: (mean ± SD)

Group	*MRR* (ms)	*MRT* (ms)	*MTpTe* (ms)
Control	849.2 ± 109.1	229 ± 16.2	88.2 ± 6.2
Athlete	1027.5 ± 124.0*	254 ± 17.6*	94.4 ± 6.9*

* $p < 0.05$.

4. Discussion

This study introduced a method to analyze the relation between TDR and cardiac cycle length in athletes and healthy sedentary controls. TDR was represented by the interval between the peak and the end of the T wave (*TpTe*-interval), as suggested by several studies reported previously [8, 12, 13, 14]. As a representation of transmural dispersion of ventricular repolarization, *TpTe*-interval is also considered a predictor of arrhythmia risk in different clinical settings [8]. Currently, a common parameter employed to assess transmyocardial ventricular repolarization inhomogeneity is the *QT*-interval dispersion (*QTd*), showing varying results across different pathologies, most of them related to *QT* measurements. This may be due either to the technical limitations in the assessments or by the *QT* correction to HR utilizing different formulas.

The analysis of the relation between VRD and cardiac cycle length has been carried out in previous studies by our group, by collecting *RR*-intervals in different histogram classes [2, 3, 4]. Therefore, the strategy of separating the *TpTe*-intervals into different *RR*-interval ranges makes it possible to study TDR dependence on cardiac cycle length without the need to use HR correction formulas. Thus, by comparing control and athlete groups, the study introduced potentially novel information that brought insights into the dependence of heart rate on TDR.

Utilization of *RT*-interval as a measure of VRD instead of the conventional *QT*-interval has been proved to be more accurate and has several computational advantages [15]. In both groups, the mean VRD measures were strongly dependent on the instantaneous *RR*-interval, confirming previous findings [2, 4]. In a physiological range of variability (600 to 1200 ms), pooled *MRT* are greater at larger *MRR* (Figure 2b). This relation held a strong linear dependence. *MRT* intra- and

inter-group comparison showed no significant differences, although athletes had higher absolute *MRT* values.

By measuring the *TpTe*-interval considering the cardiac cycle range (*MRR vs. MRT*), both groups presented surprising behavior. In Athletes, *TpTe*-interval increases as a linear function of *RR*-interval, in a wide physiological range of *RR*-interval variation at rest supine position. On the other hand, in healthy sedentary subjects, *TpTe*-interval remained approximately unchanged. The regression line slope (*sMTpTe*) found among athletes (positive slope; Figure 2a) as compared to normal sedentary volunteers (negative slope; Figure 2a) represented a pattern of cardiac electrophysiological and autonomic remodeling related to physical conditioning status, not described previously [16].

As expected, heterogeneity in the duration of the ventricular repolarization phase 3 leading to arrhythmias has been described in athlete's heart [17]. Actually, *TpTe*-interval has been found increased in athletes with myocardial hypertrophy [12]. *TpTe*-interval has also been found significantly larger in female water polo athletes as compared to healthy sedentary volunteers [13]. In long distance runners (30 km) over 50 years of age, an increase in *QTc* interval duration at the expense of *TpTe*-interval prolongation has also been reported [14].

Study limitations include a small sample size and the very strict beat selection. More specific studies are necessary to stablish whether these findings may become a tool for either physiological condition assessment or risk stratification of cardiac arrhythmias.

5. Conclusion

In well trained athletes, *TpTe*-interval is larger as compared to matched healthy sedentary subjects, and increases as a linear function of *RR*-interval in a wide physiological cardiac cycle length variation, at rest. In healthy sedentary subjects, however, *TpTe*-interval remains stable in equivalent cardiac cycle length variation range.

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Address for correspondence.
Jurandir Nadal
PO Box 68510; Zip code 21941-972; Rio de Janeiro, RJ, Brasil.
E-mail: jn@peb.ufrj.br