Comparing Six QT Correction Methods in an Athlete Population

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Abstract

Sinus bradycardia and prolonged QT interval corrected (QTc) are frequently noted on resting ECG in athletes. Possible explanation for longer QT includes inaccuracies in the correction formula. This study aimed to compare six formulas commonly used to correct QT interval duration by heart rate (HR): Bazett, Hodges, Fridericia, Framingham, linear and exponential regression. Population studied was of 1179 Caucasian people. QTc were calculated using the six formulas specified, as well as the correlation coefficients between QTc and HR. Additionally, QTc was determined for several thresholds of bradycardia (63bpm-43bpm). As expected, QTc is longer in women and in athletes ($p<10^{-4}$) for all correction formulas. QTc in bradycardia population were different from each formula: with Bazett formula, it is longer in non-bradycardia than in bradycardia group (404.10±24.6 ms vs. 384.70±24.37 ms, $p<10^{-4}$), with Fridericia formula, there was no difference between groups (394.12±24.60 ms vs. 394.71±23.89 ms, p N.S.), and with Hodges formula, it is longer in bradycardia group (393.35±22.78 ms vs. 400.35± 27.21 ms, $p<10^{-5}$). Finally, from our results, the best-adapted formula to overall thresholds of non-bradycardia is Fridericia one. Most of the correction formulas explored give an acceptable QTc approximation for a first screening in athletes. Further works should be addressed to the study of athlete's ventricular repolarization in a multifactorial way.

1. Introduction

The QT duration on electrocardiogram (ECG) reflects the duration of the depolarization and repolarization of all ventricular cells. The QT duration depends on heart rate (HR). Thus, it is recommended to correct QT duration by HR in order to propose normal values. The aim of the corrected QT interval (QTc) is to normalize the QT interval to the value that it would have if the HR were 60 beats/min (bpm). The identification of a prolonged QT interval corrected for heart rate (QTc) in athletes raises the potential diagnosis of congenital Long QT Syndrome (LQTS) and issues relating to disqualification from competitive sports [1]. Cardiovascular pre-participation screening before competitive sport, include familial and personal medical history, physical examination and 12 leads ECG. Sinus bradycardia, respiratory arrhythmia, junctional rhythm, incomplete right bundle branch block and prolonged QT interval duration are frequently noted on resting ECG in athletes.

Bradycardia is defined by HR less than 60 bpm and it is the result of a physiological adaptive change of the Autonomic Nervous System (ANS) and reflects the level of athletic conditioning [1].

Possible explanation for longer QTc in athletes includes inaccuracies in the correction formula for slow heart rates. Bazett was the first correction formula proposed [2] and it is still the most used, absolute QT interval duration is classically corrected by HR according to the Bazett's formula. After Bazett, numerous formulas have been conceived, but currently there is no consensus for the optimal formula to correct QT intervals [3, 4]. Some studies have evaluated different QT correction formulas taking into account the influence of age and gender [5, 6]. However, the validity of these formulas can be questioned on athletes where it has been shown that QT varies not only with HR but also with other factors like gender, race and the ANS modulation. However, to our knowledge correction methods have not been explored in athlete's population where heart rate is commonly less than 60 bpm.

Thus, this study aimed to compare six formulas commonly used to correct QT interval duration by HR: Bazett, Fridericia, Framingham, Hodges, linear and exponential regression, in athlete's population. These formulas are presented in the first section while results section compare gender, sedentary and athletes, and influence of bradycardia thresholds. Conclusion and perspectives are then drawn in the last section.

2. Methodology

2.1. Database

Population included 1179 Caucasian people (17 to 38 years old, 427 women, 939 athletes and 240 sedentary subjects) from multi-centric and prospective French study [7]. The athletes were all high-level trained (> 10 h/ week) and participated to national and international competitions in their discipline: badminton, handball, basketball, football, swimming, squash, rugby, hockey, table tennis, tennis, boxing, triathlon, skiing, water polo, cycling, judo, and weight lifting. A resting 12-lead ECG in supine position has been recorded in each subject. All ECG have been analyzed by the same specialist in a blind-manner concerning the two groups, trained and sedentary. RR and QT intervals duration has been measured in DII. All measurements have been made manually with a tracer table on three successive cardiac cycles. The mean value has been used for statistical analysis.

2.2. Methods

As already mentioned, several formulas were proposed in the past. In this study, six formulas were evaluated and compared, there are:

1. Bazett : $QTc_{Ba} = QT \cdot RR^{1/2}$ [1]
2. Fridericia: $QTc_{Fri} = QT \cdot RR^{1/3}$ [2]
3. Framinghan: $QTc_{Fra} = QT + 0.154 \cdot (1000 - RR)$ [3]
4. Hodges: $QTc_{Hod} = QT + 105 \cdot (1/RR - 1)$ [4]
5. Linear: $QTc_{li} = QT + K_1 \cdot (1000 - RR)$ [5]
6. Exponential: $QTc_{ex} = QT \cdot RR^{K_2}$ [6]

Where K_1 and K_2 are regression parameters estimated from RR-QT data series. The QT, QTc and RR intervals are expressed in ms. Correction formulas came from regression analysis of QT *vs.* RR. Bazett and Fridericia formulas are particular cases of exponential formula. The Hodges ones is a particular case of linear formula.

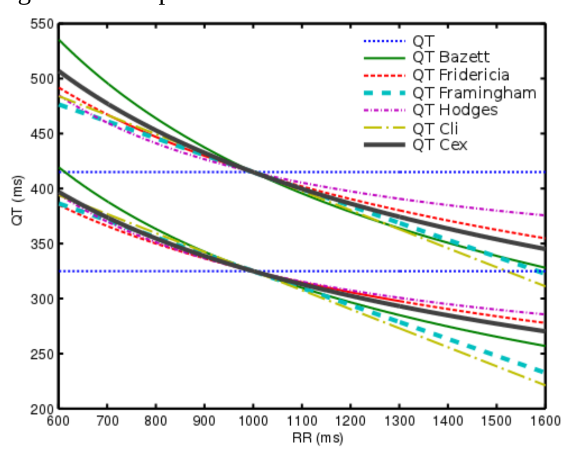

Figure 1. Six QT correction for two values of QT duration respectively 325 and 425 ms

As an example, Figure 1 shows the QT correction for two theoretical values of QT (QT1=325 ms and QT2=425 ms) for RR interval varying between 600 ms and 1600 ms. It can be observed that at low HR the difference between formulas are more important. In both cases, QT is less shortened using Hodges formula.

2.3. Statistical analysis

The QTc interval was calculated using the six previous formulas. Data were considered as mean ± SD. We studied the effects of sex (men *vs* women), age (<18 y.o. *vs.* >18 y.o.), training (athletes *vs.* sedentary), and heart rate (<60 bpm *vs;* >60 bpm). Wilcoxon rank sum test was used to determine the significant differences between groups, with a significant threshold of p<0.001. The correlation coefficients between QTc and RR were also computed. We remind that a low correlation between QTc and RR means that the influence of RR interval has been discarded. Additionally, parameter was determined for thresholds of bradycardia from 63 bpm to 43 bpm.

3. Results

Table 1. QTc men vs women

Formula	Men N=752	Women N=427	p
QT_{Ba}	387.49±25.12	406.01±24.25	$<10^{-4}$
QT_{Fi}	388.37±23.34	405.04±22.07	$<10^{-4}$
QT_{Fra}	386.25±23.91	403.77±22.34	$<10^{-4}$
QT_{Hod}	391.26±24.74	406.92±23.31	$<10^{-4}$
QT_{li}	386.92±23.66	403.81±22.25	$<10^{-4}$
QT_{ex}	388.07±23.29	405.30±22.13	$<10^{-4}$

Table 2. QTc age

Formula	> 18 year N=1119	< 18 years N=160	p
QT_{Ba}	387.74±24.98	395.10±24.20	$<10^{-3}$
QT_{Fi}	386.09±23.62	394.18±22.42	$<10^{-3}$
QT_{Fra}	385.45±22.69	395.76±22.87	$<10^{-3}$
QT_{Hod}	386.89±23.22	393.65±24.89	$<10^{-3}$
QT_{li}	387.10±23.72	394.59±23.70	$<10^{-3}$
QT_{ex}	385.25±22.09	393.31±22.95	$<10^{-3}$

Table 3. QTc sedentary people vs athletes

Formula	Sedentary N=240	Athletes N=939	p
QT_{Ba}	394.95±26.30	391.20±26.37	0.08
QT_{Fi}	396.33±23.80	386.79±24.54	$<10^{-4}$
QT_{Fra}	394.01±24.72	386.79±24.44	$<10^{-3}$
QT_{Hod}	399.31±25.07	387.52±24.37	$<10^{-4}$
QT_{li}	393.25±25.63	387.97±24.90	0.008
QT_{ex}	395.80±24.08	388.32±24.72	$<10^{-3}$

On the overall population, the mean HR was 69.96 ±

13.63 bpm; Tables 1, 2 and 3 show the differences between sex, age, and training level, respectively.

As expected, QTc is longer in women, athletes and in youth. For all correction formulas, RR interval duration was most correlated to QTc calculated using Bazett and Fridericia formulas (r=0.56 and r=0.39) whereas it was less correlated using linear and exponential formulas (r=0.17 and r=0.01). Figure 2 shows the effect of bradycardia (HR< 60 bpm) on QTc for each formula: with Bazett, Framinghan, linear and exponential formulas QTc is longer in non-bradycardia than in bradycardia group (QT_{Ba} =404.10±24.6 ms vs. QT_{Ba}= 384.70±24.37 ms, $p<10^{-4}$); with Fridericia formula, there was no difference between groups (QT_{Fi} =394.12±24.60 ms vs. QT_{Fi} =394.71±23.89 ms, p N.S.); and with Hodges formula, QTc is longer in bradycardia group than in non bradycardia one (QT_{Hod} =393.35±22.78 ms vs. QT_{Hod} =400.35± 27.21 ms, $p<10^{-5}$). Same results were observed in athletes and in sedentary subjects. QT is overcorrected with Framinghan, linear and exponential formulas and is undercorrected with Hodges one.

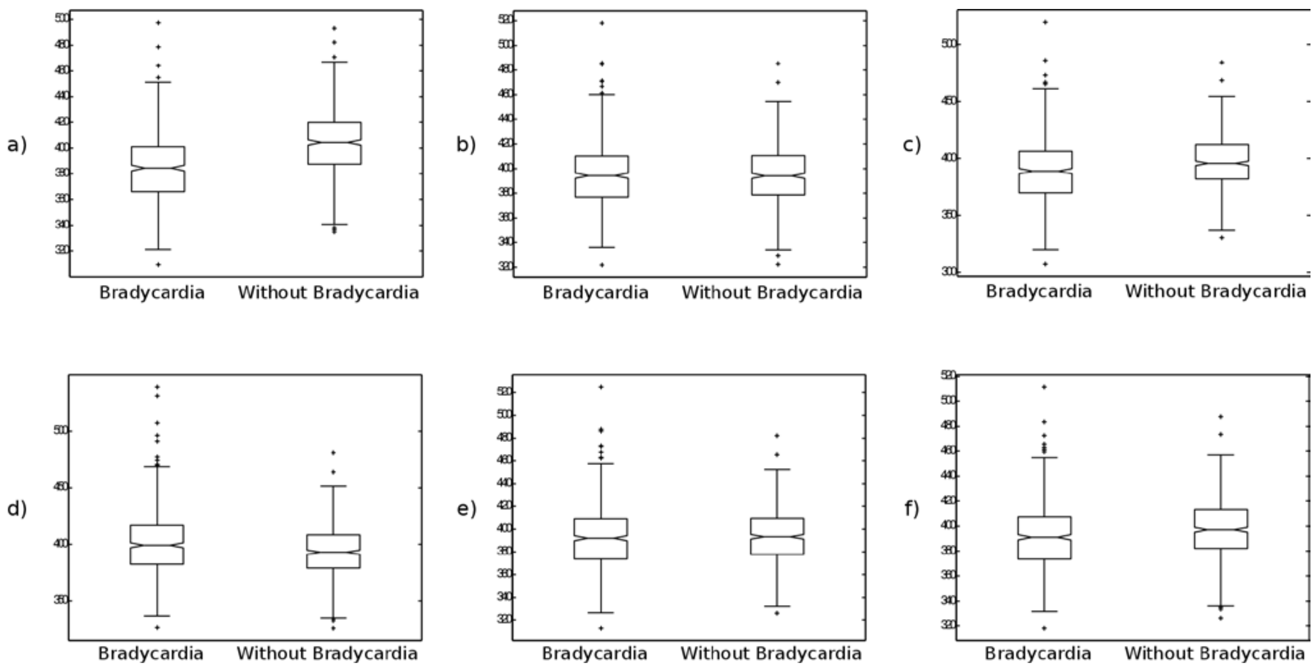

Figure 2. Correction for non-bradycardia *vs.* bradycardia population a) Bazett, b) Fridericia, c) Framingham, d) Hodges, e) linear, f) exponential.

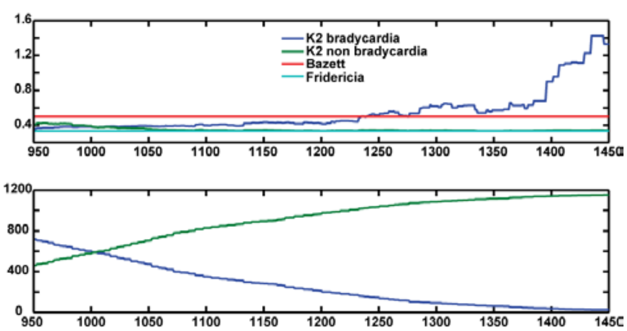

Figure 3. (top) Regression parameter K_2 for several thresholds of bradycardia (63bpm-43bpm). (bottom) Bradycardia and non bradycardia population size.

Previous works used 60 bpm as threshold of bradycardia. We also explored parameter K_2 for several thresholds of bradycardia (63 bpm-43 bpm). Results are shown in Fig. 3, until RR=1240 ms (48 bpm), values of K_2 are between Bazett (K_2=0.5) and Fridericia (K_2=1/3) values. From this threshold, K_2 for bradycardia increases rapidly. Visually, it is obvious that for non-bradycardia population, K_2 values are in the neighborhood of 1/3. It is also possible to observe that Bazett overcorrected until RR=1240 ms (both for bradycardia and non-bradycardia groups). Consequently, Fridericia formula gives a better correction of QT to overall thresholds of non-bradycardia.

Figure 4 illustrates patterns of the QT/RR and QTc/RR scatter diagrams obtained with Bazett correction for the whole population, for the women and for the men. European criteria establish that QTc is prolonged if greater than 440 ms in men or greater than 460 ms in women, using Bazett criteria. Even so, limits of QTc duration in highly trained athletes causes controversy, North-American recommendations are 470 ms in men and 480 ms in women. Furthermore, a QTc > 500 ms seems highly suggestive of long QT syndrome in athletes [8]. In the present study with the QTc European criteria we noted two male athletes with bradycardia and prolonged QTc, only one male athlete with North-American recommendations, and none case of QTc greater than 500 ms.

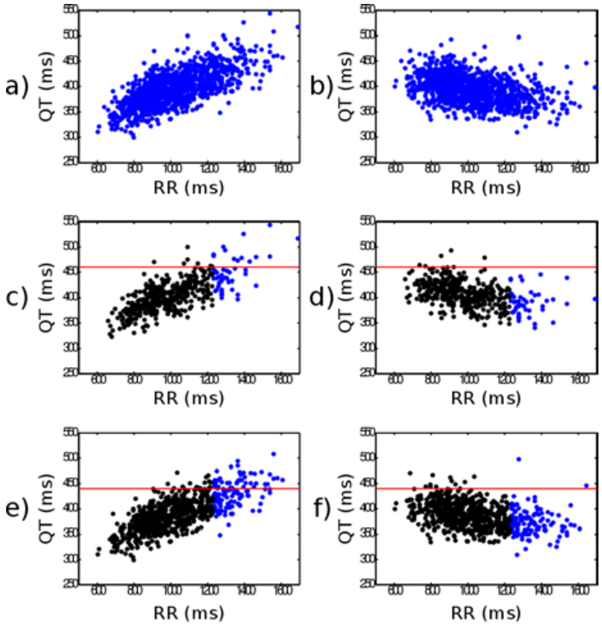

Figure 4. RR vs. QT for whole population (a), for women (c), for men (e) and RR vs. QT corrected by Bazett for whole population (b), for women (d), for men (f). Red lines represent the upper limits of QTc proposed by European Society of Cardiology, respectively 440 ms for men and 460 ms for women.

4. Conclusions and future work

In a clinical context, diagnosis of long QT duration and issues relating to disqualification from sporting disciplines are important. In this study we have explored six different QT correction formulas in two populations, athletes and sedentary people. Our results showed that most of the correction formulas explored give an acceptable QTc approximation for a first screening in athletes, even it has been shown that classical formulas are not adapted for low heart rates (below 48 bpm). However, a formula may lead to overcorrection or/and undercorrection for certain HR boundaries, making the differences more or less evident in the limits of low and high heart rates. Indeed, Bazett's formula, the most used formula in cardiology, overcorrected at high heart rates and undercorrected at low heart rates. Fridericia formula seems the best adapted whatever the level of HR. Changing bradycardia's thresholds can be tempted to propose new formulas for different threshold correction using linear or exponential regression. Therefore a new correction formula is impractical, not necessary and its contribution for the detection of prolonged QT in case of marked bradycardia will be not significant. It is essential to focus on defining the limits of normal electrocardiographic's parameters in athletes, to better recognize a pathological long QTc. It was not possible to establish the limits of a long QT interval from this population, knowing that their prevalence, according to European criteria, is less than 0.17% (16/939) [7]. In this study the number of QT long remains unspecified, current work is directed towards the evaluation of these correction formulas on a large and annotated database. Since QTc prolonged in the absence of symptoms is not an indication for LQTS [8], further works should be addressed to the study of athlete's ventricular repolarization in a multifactorial way, taking into account: genetic, training specificities, anthropometry, gender, age and ethnicity.

Acknowledgements

This work has been supported partially by the Simón Bolívar University DID and by ECOS NORD cooperation program.

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