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Comparative study of three methods for QT interval correction in African national level football players
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Comparative study of three methods for QT interval correction in African national level football players

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The aim of this study was to compare three correction methods of QT interval in African national level football players. QT interval was measured in D2 lead on resting electrocardiogram (ECG) in 216 Black male football players (age range 18 to 35 years). Corrected QT (QTc) was calculated using Bazett, Fridericia, and Framingham’s formulas. Means and percentages of long QT (QTc≥440 ms and QTc≥470 ms) and short QT (QTc≤320 ms) were compared. Correlations and agreement criteria between correction methods were researched, and effects size were calculated. Heart rate was 59±9 beats/min (40 to 84) and measured QT (QTm) at 383.1±31.4 ms (320 to 480). QTc were 378.9±25.7, 380.1±23.8, and 383.1 ± 31.3 respectively with Bazett, Fridericia, and Framingham formulas; differences were not significant. According to the definition QTc>440 ms, no long QT was found using Fridericia formula whereas Bazett and Framingham showed 1.4% of long QT. Only Framingham's formula showed long QT according to the definition QTc≥470 ms (0.9%). Framingham’s formula also showed significant difference with short QT as compared to the other methods (5.1 vs. 0.46%; p=0.008). The lower QTc value was 320 ms in all methods. Correlation and agreement were better between Bazett’s and Fridericia’s formula. Framingham's formula showed higher proportions of long and short QT, while Fridericia's one reduced them. Bazett's formula gave intermediate percentages. QTc<320 ms could be used to define short QT; 320 ms representing the lower limit in our study for the 3 formulas. Our data did not allow us to deduce a definition for the long QT. The limits of QTc ≥ 470 ms for men and QTc ≥ 480 ms for women, more adopted now in the literature, were suggested.

Key words: QT interval, electrocardiogram, football player, Bazett, Fridericia, Framingham.

INTRODUCTION

Electrocardiogram (ECG) is a simple and practical diagnostic tool whose usefulness is recognized in athletes, particularly in preparticipation screening for cardiovascular diseases. The signs observed in athlete’s ECG continue to be discussed in order to determine proven abnormalities and those are worth monitoring.
Analysis of ST segment, T wave and QT interval during repolarization hold an important place in the interpretation. ST segment and T wave changes may evoke a coronary disease among others. The duration of the QT interval varies with heart rate (HR); therefore, the measured QT (QTm) is adjusted, to give the corrected QT (QTc). Various correction methods are proposed and normal QTc limits vary according to recommendations (Corrado et al., 2010; Drezner et al., 2013). The choice of the appropriate method and the good interpretation of results are crucial to avoid wrongly disqualifying athlete or to miss out on a potentially serious abnormality.

Standards have been proposed for QTc on the basis of which studies have been conducted to exclude athletes from certain competitions (Moss, 2007). Short or long QTc can be responsible in short-term of major rhythm disorders as torsade de pointes, source of syncope and sudden death (Gaita et al., 2003; Viskin, 1999). These abnormalities can be congenital in relation to the mutation of genes encoding for cardiac potassium and sodium channels (Brugada et al., 2004; Cercone and Priori, 2011; Schwartz et al., 2006) or induced by medication (Shah, 2010; Zaręba, 2007). An heterogeneity has been noticed in the genetic presentation (Borggrefe et al., 2007; Lehnart et al., 2007; Wolf and Berul, 2008).

Football is one of the most practiced sports in the world with huge financial stakes. Almost all countries organize regular championships and participate in international competitions managed by structures in place for decades. Players on the field are not safe from serious cardiac events whose source may be an abnormal QT interval duration. Among accused trigger factors, figure a high intensity physical exercise.

The aim of this study was to conduct a comparative analysis of the QTc duration in national level Black African football players, applying three of the most currently used correction formulas in the literature.

**SUBJECTS**

Participants were male football players from several of the Senegalese premier league championship teams. Football players had an average of 8 to 10 h of training weekly, were all Black, and aged between 18 and 35 years. They all at least played since junior category, were well trained and included in the study 4 months after the beginning of the championship season. None of them had a known cardiac disease and was taking medication at the time of the study. Explanations on the purpose were allowed to obtain the free consent from participants. This study was approved by the Institutional Ethic Committee of the University Cheikh Anta Diop of Dakar. The study was conducted in accordance with the Helsinki Declaration as revised in 1989.

ECG recording was carried out on an appropriate table for examination using an electrocardiograph (Cardioline Delta 60 Plus, Remco Italia). During physical examination, we emphasized on a correct measurement of blood pressure by a stethoscope and an aneroid sphygmomanometer (Spengler EC 0459, France) calibrated in mmHg

**METHODOLOGY**

Clinical examination started in clubs’ headquarters without pre-established order after at least 10 min of rest. It included an anamnesis on civil status, existence of possible symptomatology and a physical examination focused on the cardiovascular and respiratory systems. The 222 examined subjects benefited then from a 12-lead ECG recorded at rest, in extended position. The unwinding speed of the paper was at 25 mm/s. A calibration of 10 mm for 1 mV in ordinates and 1 mm for 4/100 s in X-coordinates was adopted. Each tracing, in addition to 12 traditional leads, had a long D2 lead recording. Three leads were registered simultaneously: standards (DI, DII, and DIII), unipolar limb leads (aVR, aVL, and aVF), precordials (V1, V2, and V3) and (V4, V5, and V6). ECGs of 3 football players were not included because they had a high systolic blood pressure (SBP). A blood pressure above normal values was defined as a SBP ≥ 140 mmHg and/or a diastolic blood pressure (DBP) ≥ 90 mmHg. None of the 219 remaining ECG showed a ventricular or supraventricular rhythm disorder. There were neither intraventricular conductive disorders nor signs of pre-excitation. Three cases of 2nd degree atrioventricular block stage 1 of Mobitz were removed. We were thus able to examine 216 ECG tracings. The interpretation made by the same cardiologist who conducted examinations and performed ECG, was focused on the repolarization, and precisely on QT interval. The duration of measured QT interval (QTm) was taken manually on D2 lead from the onset of QRS complex and the point where the descending limb of the T wave intersects the isoelectric line. Tangent method was used if the end of T wave was not clearly defined. The corrected QT (QTc) was next calculated using the interval between 2 consecutive R waves (RR) preceding the measured QT. Applied formulas for correction were those of Bazett (QTc=QTm/√RR), Fridericia (QTc=QTm/(RR)^1/3) and Framingham (QTc=QTm+0.154(1-RR)). QTm and QTc were expressed in milliseconds and RR in seconds. The definitions used for long QT were that of European Society of Cardiology (ESC) revised (Corrado et al., 2005; 2010), that is, QTc ≥440 ms and the Seattle criteria for interpretation of ECG athletes, that is, QTc≥470 ms (Drezner et al., 2013). One definition of short QT was chosen, QTc≤320 ms (Drezner et al., 2013).

**Statistical analysis**

Statistical evaluation was carried out using the software Sigma Stat 3.0. Data were expressed in means ± standard deviation. The found mean values of QTc according to various formulas were compared using the One way analysis of variance (ANOVA). When the normal

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test failed, it was replaced by the Kruskal-Wallis on ranks. The existence of long and short QT was researched. If necessary, the percentages obtained according to formulas were compared using Z-test. In order to assess the agreement between correction methods, the variance coefficient was calculated, Pearson correlation and Bland-Altman test were also used. The magnitude of differences was evaluated from the calculation of Cohen’s d effect sizes. A significant difference was admitted for p<0.05.

RESULTS

The mean age of football players was 23.1±3.1 years, mean heart rate of 59±9 beats/min (40 to 84) and mean blood pressure 117.8±7.3 mmHg (100 to 130) for SBP and 72.2±6.5 mmHg (60 to 80) for DBP. The mean QTm was 383.1±31.4 ms (320 to 480). Their weight, height, and body mass index (BMI) were respectively 69.5±1.1 kg (54 to 88), 178.9±6.4 cm (163 to 198), and 21.6±1.5 kg/m² (18.1 to 25.6). 116 cases (53.7%) of sinus bradycardia were found. There was no significant difference between mean values of QTc obtained according to the different formulas. Only Framingham formula gave 2 cases of QTc>470 ms. Remarkable fact, it also showed 18 cases (8.3%) of QTc equal to 440 ms (439.9 ms precisely). The lower extreme value of QTc was 320 ms for all formulas, allowing to obtain 11 cases of short QT according to Framingham and 1 case for each of the other formulas with significant difference. The mean QTc values, percentages of long and short QT within limits and p values in comparison between formulas are shown in Table 1.

There was a negative but not significant correlation between the heart rate on one hand and mean values of QTc on the other hand (Figure 1).

The pair Bazett-Fridericia (A vs. B) showed the smallest variance coefficient and effect size, but the higher level of positive correlation as given in Table 2. The opposite was found between Bazett and Framingham (A vs. C) for the variance coefficient and the effect size.

An analysis of Bland-Altman plots represented in Figure 2 highlighted the smallest bias in absolute value between Bazett and Fridericia (-1.1) and the higher one between Bazett and Framingham (-4.1). The former couple of formulas also gave the narrowest interval in which almost all the differences were included (from +1.96 SD = -6.4 to -1.96 SD = +4.1).

DISCUSSION

Choice of the lead for QT measurement

Classically, leads D2 or V5 are used for the manual measurement of QT interval. The end of the T wave is supposed to be the clearest in these leads (Mönig et al., 2006). The lead D2 has been chosen for the whole of measurements in this study. Other recommendations were made by the American Heart Association (AHA) experts (Rautaharju et al., 2009): (1) When QT interval is measured in leads recorded from single channel, the lead showing the longest QT should be used. It is usually V2 and V3; (2) If the T wave and U wave are superimposed or cannot be separated, it is recommended that measurement should be made in the lead showing no U waves, often aVR and aVL. In the other hand, the downslope of the T wave can be prolonged by tracing a tangent until its intersection with TP segment. However, it has been admitted that defining the end of T wave in this way could underestimate QT interval.

Heart rate

The mean HR was 59±9 beats/min. Sinus bradycardia was found in many football players in the population of this study (53.7%). It represents one of the characteristic signs of modifications known as "athlete’s heart" and is more observed in endurance sports training. It can be related to a reinforcement of the vagal tone. Considered as a sport with low static and high dynamic components as proposed by Mitchell et al. (2005), football can justify this HR decrease at rest.

The various formulas

Considering the whole values of QTc for the 216 football players, there was no significant gradual decrease in results obtained successively according to Bazett, Fridericia, and Framingham formulas. Bazett’s formula gave the lowest mean QTc value. In the literature, Bazett’s formula is the most commonly used, privileged particularly in Italian and European studies in general. In their proposals, the experts of the AHA argue that the
correction formulas like Framingham using the linear function of RR or HR are preferable to Bazett or Fridericia. The principal reason is that these last two formulas lead to QTc values that can be erroneous especially in the highest HR. In general, Bazett's formula is considered useful in normal HR range, but tends to underestimate the duration of repolarization in low HR and to over-estimate it in high one (Vetter, 2007).
Table 2. Parameters of agreement between correction methods.

<table>
<thead>
<tr>
<th>Variable between formulas</th>
<th>Bazett = A vs./and</th>
<th>Fridericia = B</th>
<th>Bazett= A vs./and</th>
<th>Framingham = C</th>
<th>Fridericia= B vs./ and</th>
<th>Framingham = C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean QTc (ms)</td>
<td>(A+B)/2=379.6±24.8</td>
<td></td>
<td>(A+C)/2=381±28.2</td>
<td></td>
<td>(B+C)/2=381.6±27.3</td>
<td></td>
</tr>
<tr>
<td>Variance coefficient (%)</td>
<td>6.5</td>
<td></td>
<td>7.4</td>
<td></td>
<td>7.1</td>
<td></td>
</tr>
<tr>
<td>Correlation</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>r</td>
<td>0.997</td>
<td>0.995</td>
<td>0.953</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>p value</td>
<td>4.07 e-240</td>
<td>1.995 e-115</td>
<td>8.24 e-113</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Effect size (%)</td>
<td>2.4</td>
<td>7.3</td>
<td>5.4</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

According to the ESC recommendations, the HR should be >40 beats/min without exceeding 120. These recommendations were in line with our study population whose HR ranged between 40 and 84 beats/min. In Seattle criteria, an ideal HR interval is fixed between 60 and 90 beats/min. A systematic gradual relation was not found between heart rate and QTc, because the QTm intervene in equations can vary between subjects particularly when an abnormal repolarization existed.

Our results highlighted better agreement between Bazett’s and Fridericia’s formulas through the lower dispersion around the mean (6.5% of variance coefficient), the smallest effect size, mean of differences, and limits of agreement. In general, there was good correlation between formulas, particularly Bazett and Fridericia. Using Cohen’s benchmarks (small: 0.2, medium: 0.5 and large effect: 0.8), the effects size were all small, enhancing the value of non significant differences observed with the ANOVA test. The level of agreement between Bazett and Fridericia was not surprising, because equations are based respectively on the square and cubic root of RR.

Standard values of long QT

In the European consensus (Corrado et al., 2010) based on the Italian experience using Bazett’s formula, long QT is defined as QTc>440 ms in men and >460 ms in women. In a study carried out in the United Kingdom among top athletes (Basavarajiah et al., 2007), 7 of them (6 men and 1 woman) had a long QT, and 3 had basic QTc>500 ms. The 7 athletes in question were asymptomatic and did not have family history of long QT congenital syndrome (LQTS). Five of them agreed to be subjected to a genetic testing, and only one had a positive diagnosis with abnormality on the gene KCNQ1. The population consisted of 2,000 subjects, including 520 football players (26%); other representative disciplines were rugby, tennis, and swimming. Their mean HR was 58 beats /min (range: 47 to 68). Other limit values have been recommended by AHA experts, that is, 450 ms or more in men and 460 ms or more in women. In a population of 150 Nigerian athletes (128 men and 22 women) composed by 100 practitioners in dynamics and 50 in statics, Lawan et al. (2008) found 1.3% of long QT based on recommendations of the 36th Bethesda Conference (Maron and Zipes, 2005; Pelliccia et al., 2008), that is, QTc≥470 ms in men and ≥480 ms in women. In this study, 1.4% of QTc>440 ms according to Bazett and Framingham, and none from Fridericia were registered. Considering the evolution of studies in sportive domain, the limit of 440 ms is less adopted to define the long QT in favor of a QTc value at least equal to 470 ms (Ubero et al., 2011). This value allowed Wilson et al. (2012) to find 1 case (0.3%) of long QT among 300 national level Black African athletes; their mean QTc according to Bazett was 391.5±25.9 ms (range: 330 to 470). The Seattle criteria adopted the same limit. A comparison between these criteria and the ESC recommendations permitted Sheikh et al. (2014) to propose refined criteria that can significantly reduce the number of false-positive ECG in athletes as well as Arabs, Blacks than Caucasians (Riding et al., 2015). In patients (Johnson and Ackerman, 2009) as well as in athletes a QTc>500 ms suggests highly a diagnosis of long QT especially if it goes with cardiac events like episodes of ventricular tachycardia and syncope. None of our football players presented a QTc≥500 ms. According to Moss (2007), it is careful to recommend the non participation in competitions to athletes reaching this level. He also established a limit area which should not constitute a reason for competitive athletes’ disqualification apart from other arguments in favor of the long QT or a proved cardiac disease. It is a QTc ranging between 460 and 500 ms, these two values being excluded. In our study, only Framingham’s formula has given values in this level; the maximum obtained by Fridericia and Bazett was respectively 432.8 and 450.2 ms.

Standard values of short QT

The literature is full of works about long QT in athletes,
Figure 2. Bland-Altman plot of QTc differences between two formulas vs. mean QTc of these formulas. Formulas are Bazett=A, Fridericia=B and Framingham=C. Up to down are represented differences: (A-B), (C-A) and (B-C). Means into graphics (-1.1, -4.1 and -3) are the bias. Limits of agreement (dotted lines) go from -1.96 SD to +1.96 SD.

but less data are available for the short QT although it is also recognized as causing cardiac events and family sudden death (Gaita et al., 2003; Gussak et al., 2000). Like for the long QT, there is no unanimity on the
reference value to clarify the definition. The ESC (Corrado et al., 2005) proposed QTc<300 ms, while other authors indicated a value <320 ms (Couderc and Lopes, 2010; Schimpf et al., 2005). In a middle-age population from Finland, Anttonen et al. (2007) found 0.1% of QTc < 320 ms according to Bazett and 0.08% by Fridericia on ECG of 10822 randomly selected subjects. He also showed that short QT was not systematically associated with cardiac events. Eleven of our football players (5.1%) had a QTc equal to 320 ms according to Framingham method with a significant difference compared to other formulas where 0.46% is noted. The limit of 300 ms may restrict the short QT diagnosis; in a randomized trainings analysis of over 100000 patients, Reining and Engel (2007) did not find any one.

Conclusion

This study population has the advantage to be homogeneous, made of male Blacks athletes, who practice the same discipline, the football, but needed to be enhanced. Extreme levels of the corrected QT interval, higher or lower, can be the starting point of cardiac arrhythmias and lead to sudden death, a tragedy if it specially occurs in a young athlete. In our study, the application of Framingham’s formula leads to higher proportions of QTc judged short or long. It thus tends to exaggerate the extreme values while Fridericia’s one tends to reduce them. Bazett’s formula gives intermediate proportions of abnormal QT and the lowest mean values of QTc at low to medium level of HR: it can be used in the ECG interpretation for athletes whose practice include a strong dynamic component like football. A QTc strictly inferior than 320 ms could be used to define short QT; with 320 ms representing the lower limit in our study for the 3 applied formulas. On the other hand, the data of this study did not allow us to deduce a definition for the long QT. So, the limits of QTc ≥ 470 ms for men and QTc ≥ 480 ms for women, more adopted now in the literature, are suggested.

Conflict of Interests

The authors have not declared any conflict of interests.

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