



Rapid Communication

Criteria for short QT interval based on a new QT-heart rate adjustment formula

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ABSTRACT

Background: A short QT interval, within which an increased risk for atrial fibrillation and/or fatal cardiac arrhythmias occurs, has been difficult to define.

Methods: The lower percentiles of a new QTc formula were determined, using a precise mathematical fitting of the QT-heart rate relationship from the ECGs of 13,600 individuals from the NHANES II and III surveys.

Results: The QTc interval for persons in the lower fifth percentile, second (2.5th) percentile and first percentile, were calculated.

Conclusions: Based on the new spline formula, a short QTc is defined at the first percentile, and is less than 380 ms in both men and women.

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1. Introduction

A short QT interval on the electrocardiogram identifies individuals with a high risk for the development of atrial fibrillation and/or fatal cardiac arrhythmias [1,2]. However, questions about the prevalence of this condition have been difficult to answer [3–10]. The difficulties with identifying this condition are several-fold including determining the diagnostic criteria and selecting the appropriate QT heart rate adjustment formula.

Heart rate is well-recognized to affect the QT interval, necessitating the application of a heart rate correction formula (QTc). The Bazett formula is used by most studies and guidelines to define the short QTc [4–6,9–11]. Unfortunately, this formula is only satisfactory when applied in cases involving a heart rate of around 60 bpm; it becomes progressively less accurate at faster and slower heart rates [12]. Recently, a new QT-heart rate correction formula was developed based on the ECGs from about 13,600 individuals in the United States' National Health and Nutrition Examination Survey (NHANES) population study, and was shown both to be relatively independent of heart rate and also superior to other formulae [13]. However, it was used to evaluate long QT intervals [13], the other part of the QT spectrum, short QT interval, was not considered. Thus, the purpose of this current study was to define the QT interval limits that constitute a short QT interval.

2. Material and methods

The methodology to construct the new QTc has been presented in detail [13]. Briefly, a spline correction function, modeled using a cubic regression spline with four knots and an adjustment for gender, was fit to the QT and heart rate ECG data of 13,600 individuals involved in the US NHANES II and III studies, conducted by the US Centers for Disease Control and Prevention (CDC) [13]. Considering the persons' ages, the spline QT correction, was developed, with each observation weighted by the respective NHANES sampling weight with spline parameters selected as those that minimized the least squares estimate fit of the QT-heart rate relationship [13]. The ECG exclusion criteria were ECG abnormalities that made the calculation of the QT interval difficult, such as left or right bundle branch block; or the presence of left ventricular hypertrophy, myocardial infarction or if rhythm was not in sinus. The heart rate and QT interval measurements were made by a computerized ECG analysis algorithm, which eliminated intra-observer variability [13].

3. Results

The QTc duration in the fifth percentile is relatively stable across all ages, until the age of 85 years, when there is a rise in men and an apparent reduction in women (Fig. 1). These changes in the older age groups of both genders are most likely due to the

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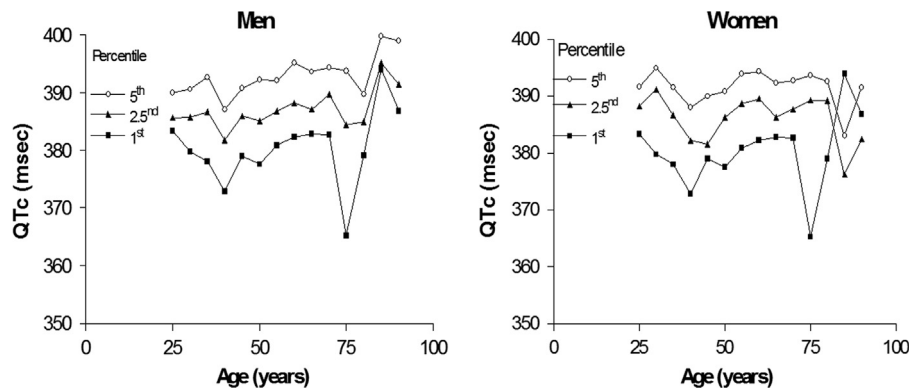


Fig. 1. The fifth, second (2.5th) and first percentile of the QT is shown across age groups from 25 to 94 years of age. Each point represents all individuals in a four-year age group, starting from 25 to 29 and ending at 90 to 94 years of age.

presence of a smaller part of the population at the older age being in the lower percentile of the QT-heart rate correction. The mean QTc for the fifth percentile was 391.2 ms for men and 391.5 ms for women. The QTc duration in the 2.5th percentile was similar, being relatively stable across all ages until the age of 85 years, when there is also a rise in men and an apparent reduction in women. The mean QTc for the 2.5th percentile was 385.8 ms for men and 386.1 ms for women. The QTc duration in the first percentile is relatively stable across all ages until the age of 75 years. The greater variability observed at the older age group is most likely due to the smaller number of the population at the older ages. The mean QTc for the first percentile was 379.6 ms for men and 370.3 ms for women.

4. Discussion

This study is the first to define the short QT interval based on a new QTc formula that is relatively independent of the effect of heart rate on QT, and does so from a large population base using statistically defined criteria.

Previous suggestions for a criterion for short QT interval have varied between different recommendations. A QTc of 390 ms and shorter has been proposed by an American Heart Association committee [14]. This would be consistent with the fifth percentile of the spline QTc. A QTc \leq 340 ms has also been proposed, based on data from cases with a short QTc that in addition also had a personal and/or familial history of cardiac arrest [15]. The proposal that short QT syndrome can be diagnosed in the presence of a QTc $<$ 360 ms and one or more of the following—a pathogenic mutation, a family history of short QT syndrome, a family history of sudden death at age \leq 40, and/or survival following a ventricular tachycardia/fibrillation episode in the absence of heart disease [8]—constitutes a multivariate definition of which QTc is only one criteria. Values of 360 or smaller would be considerably less than the first percentile using the spline QT correction formula. In the absence of the other criteria, a short QT of less than or equal to 330 msec has been proposed [8]. The Seattle criteria for the ECG evaluation of athletes suggested a criteria for short QT at an interval of \leq 320 ms [16]. Other studies have considered a QT \leq 300 ms as a short QTc [5,7,10,11]. Recognizing the percentile distributions may explain, at least in part, why four studies with a total of 266,035 persons did not identify a single case with a short QTc [5,7,9,11].

Short QTc has been calculated from the Bazett formula in most of the studies available [4–6,9–11]. However, it should be noted that the QTc based on the Bazett formula is known to undercorrect the QT interval at fast heart rates and overcorrect at slow heart rates, as compared with other correction formulae [12]. Thus, utilizing the Bazett formula for QT-heart rate correction has the

potential for error, and therefore may obscure the identification of the short QTc syndrome. In contrast, the new formula effectively eliminated differences due to heart rate, with only some small random variability [13].

It important to point out that the new QTc formula incorporated both an age and gender correction. This correction effectively eliminated differences due to age and gender, so the percentiles are approximately equal, with some small random variability, in men and women [13].

5. Conclusion

These data presented an objective criterion to identify individuals with a short QT interval by setting the first percentile as the criterion to begin the clinical search for reversible factors that might shorten the QT interval, or identify individuals with an inherited abnormality that predisposes them to arrhythmias. An applet to compute the spline QTc from user input is available at https://elenaszefer.shinyapps.io/qtc_nhanes_spline. The applet is easy to use, so that QT intervals that are of concern to the clinician can be readily entered. The QTc will be calculated along with the percentile rank of the value. The use of percentile distribution also provides a framework to evaluate the literature on other proposed criteria for short QT syndrome.

Conflicts of interest

Grant funding

The author declares no conflict of interest related to this study. There are no conflicts of interest or any relationship with industry and financial associations that might pose a conflict of interest.

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