Evaluation of QT Interval Correction Methods in Normal Pediatric Resting ECGs

H Qiu[1, 3], GL Bird[1, 2, 3], L Qu[1, 3], VL Vetter[1, 3], PS White[1, 3]

Departments of [1]Pediatrics and [2]Anesthesiology and Critical Care Medicine, University of Pennsylvania, PA, USA
[3]The Children's Hospital of Philadelphia, PA, USA

Abstract

Different methods for heart rate correction of QT intervals have been proposed, but the classic Bazett method remains widely used in current clinical practice, despite being often criticized for limitations and disadvantages. To investigate the value of commonly employed methods in pediatric patients, we evaluated four QT correction methods (Bazett, Fridericia, Framingham and Hodges formulae) in a set of 2,170 normal pediatric resting ECGs.

The dataset (age 0 to 20 years) is typical of a pediatric population for age, gender and heart rate. Scatter plotting of uncorrected QT versus heart rate reveals curvilinearity not typically identified in previously reported adult normal ECG datasets. Among the four algorithms tested, corrected QT (QTc) values calculated from the Bazett formula yielded the most consistent results across different ranges of heart rate and age. Further statistical regression modeling demonstrated that the Bazett method better fits the overall curvilinear trend in QT-heart rate distribution than the other formulae. The Bazett method also has the least residual heart rate dependence after correction.

This study provides support for the use of the Bazett QT correction method over others in normal pediatric resting ECGs. The Bazett method may represent a balance point of accuracy, simplicity and generalizability not yet surpassed by other commonly applied alternatives. Our analysis suggests that its use in general pediatric patients is appropriate as a current best option.

1. Introduction

The QT interval is an important parameter of surface resting electrocardiograms (ECG). Perturbation of its duration may predispose patients to arrhythmia and sudden cardiac death. It is well established that QT interval is inversely correlated with heart rate. QT interval is usually corrected relative to heart rate to allow interpretation of the QT interval independent of heart rate variability. Since Dr. Bazett introduced the first QT correction formula in 1920 [1], numerous alternatives have been proposed. However, convergence to a universal standard has not yet occurred. In current clinical practice, the Bazett formula is most commonly used, while the Fridericia [2], Framingham [3] and Hodges [4] formulae are less commonly employed.

Despite its wide application, the Bazett formula's scientific rationale is not well clarified, and pediatric evidence to support its utilization is lacking. It has been repeatedly criticized for perceived limitations and disadvantages, giving an impression that its popularity is mainly because of its historical precedence and simplicity [5-7].

Several studies have evaluated different QT correction methods in specific large sample populations. In a study of 10,303 adult normal ECGs, the Hodges method was preferred by Lou and colleagues [5] as the QT interval best fit a linear relation with heart rate. In a study of ECGs from 5,939 adult healthy subjects, the Fridericia method was determined to yield a more consistent QTc across groups exhibiting different heart rates [8]. The Fridericia method outperformed the Bazett method in a large set of 2,288 pediatric subjects, but these were 6 to 17 year olds enrolled in ADHD clinical trials [9]. In each case the conclusions in favor of any specific correction method were in part attributable to specific characteristics of the individual study populations, as well as the particular preference assessment criteria used.

This study was performed to compare effectiveness of commonly used QT correction methods in a broad population of general pediatric patients. Our hypothesis is that large scale automated analysis can be retrospectively applied to a set of normal pediatric resting ECGs (patients aged from birth to 20 years) to suggest preference for one QTc correction method over others.

2. Methods

A convenience sample of 2,170 normal standard 12-lead digitized ECGs (recorded between year 1991 and 2006) were retrospectively collected from the clinical information system at the Cardiac Center of the Children's Hospital of Philadelphia. At the time of initial recording, all ECGs (sampling rate of 500 Hz, paper speed of 25mm/s) are analyzed by the Marquette 12SL ECG analysis program (GE Healthcare), and each individual initial reading is then confirmed or corrected by a board-certified attending pediatric cardiologist. Only those ECGs confirmed as normal by the automated analysis and expert review processes were included in this analysis. ECGs with important electrocardiographic abnormalities confirmed on expert review were excluded. Age and gender, as well as heart rate and QT interval (values confirmed by the expert reviewer) were used for this study. We analyzed information based upon heart rate [5], rather than its oft-quoted correlate, R to R interval. Heart rate (beats per min) = 60 (sec/min)/RR (sec/beat).

We evaluated four QTc calculation methods [5]:

Bazett: $QTcB=QT/(60/HR)^{\wedge 1/2}$

Fridericia: $QTcFri=QT/(60/HR)^{\wedge 1/3}$

Framingham: QTcFra=QT+154(1-60/HR)

Hodges: QTcH=QT+1.75(HR-60)

All statistics and figures were performed using version 2.4.0 of the R statistical package (www.r-project.org).

3. Results

Our dataset of 2,170 ECGs includes a broad representation of the age, gender, heart rate and QT interval ranges seen in a large pediatric academic medical center (Table 1). The correlation coefficient is -0.92 between QT interval and heart rate, -0.74 between heart rate and age and -0.77 between QT interval and age. As expected, QT interval is inversely correlated with heart rate and age, while heart rate also correlates with age.

Table 1. Heart rate and QT interval stratification by age and gender

Age	Sex	n	HR*	QT*
0	F	89	137 ± 14	278 ± 18
	M	120	137 ± 17	282 ± 24
	Both	209	137 ± 16	280 ± 22
1-5	F	292	104 ± 17	318 ± 27
	M	293	102 ± 17	320 ± 26
	Both	585	103 ± 17	319 ± 27
6-10	F	288	83 ± 15	359 ± 27
	M	246	82 ± 15	360 ± 27
	Both	534	83 ± 15	359 ± 27
11-15	F	341	74 ± 12	380 ± 26
	M	246	74 ± 12	380 ± 26
	Both	587	74 ± 12	380 ± 26
16-20	F	180	73 ± 10	384 ± 27
	M	75	69 ± 11	386 ± 33
	Both	255	72 ± 10	385 ± 28
All	Both	2170	90 ± 24	349 ± 43

*HR (bpm) and QT (msec) values are mean ± SD

QTc values calculated from the four evaluated formulae are shown in Table 2. The Bazett formula demonstrates the narrowest range of values across age and gender groups. Among all groups, the minimum QTcB is 410 msec, maximum QTcB is 423 msec and the difference is 13 msec. The corresponding differences found for QTcFri, QTcFra, QTcH are 45, 47 and 23 msec respectively. Notably, gender variability for QTcB reached statistical significance only in the 16-20 year age group ($p<0.00001$, t-test).

Table 2. QTc calculations

Age	Sex	QTcB	QTcFri	QTcFra	QTcH
0	F	418±18	364±16	363±14	412±16
	M	423±22	369±22	367±19	416±18
	B	421±20	367±20	366±17	415±18
1-5	F	415±19	379±18	381±16	395±16
	M	413±16	379±15	381±14	393±13
	B	414±18	379±17	381±15	394±15
6-10	F	418±19	397±16	399±15	399±15
	M	417±17	396±15	398±14	398±14
	B	418±18	397±16	398±14	399±15
11-15	F	419±16	405±14	406±13	405±14
	M	418±20	405±17	406±16	404±16
	B	418±17	405±15	406±14	404±15
16-20	F	423±20	409±19	410±18	408±18
	M	410±19	402±21	403±19	401± 21
	B	419±21	407±20	408±19	406±19
All	B	417±18	393±22	394±21	401±17

Values shown as mean ± SD. B: Both

Next, we examined the distribution of uncorrected QT intervals versus heart rate. In Figure 1, a single uniform scatter plot (of uncorrected QT interval versus heart rate, n=2,170) is shown superimposed on top of each of four different sets of contour plots. Each of the four QTc correction methods we analyzed yields a different pattern of underlying contour lines. A contour line is composed of points (QT, HR) which have equivalent QTc values as calculated by a formula. For example, points (346, 80) and (384, 65) will both result in a QTc of 400 msec if calculated by the Bazett formula. Visual inspection (of the scatter plot relative to each set of contour lines) shows that the linear Hodges formula can not simulate the curvilinear nature of the QT-HR distribution. The contour lines for the Fridericia and Framingham formulae do not fit well with the curvature of the QT-HR distribution. The Bazett method's contour lines align most closely with the trend of the QT-HR distribution.

The QTc formulae are derived from regression modeling of the relationship between QT interval and heart rate. In Table 3, Model 1 is a generic parabolic model in form of $QT= \beta\times(RR)^{\alpha}$; both the Bazett (model 2) and Fridericia (model 3) methods are special cases of this model, where α are 0.5 and 0.33 respectively. Model 4 is for Framingham correction method (a hyperbolic function of HR). Finally, model 5 is for Hodges formula (a linear function of HR).

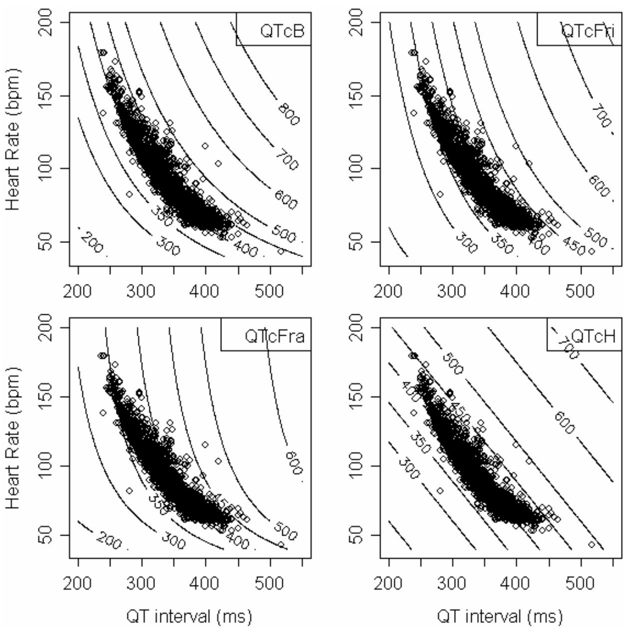

Figure 1. Scatter plot of uncorrected QT versus HR projected on contour lines for each of the four QT correction methods.

Regression analyses were performed on the 2,170 records (Table 3). We used residual standard error (RSE) and a QTc-HR correlation coefficient to quantitatively assess the four formulae. Residue is defined as the difference between the QT interval predicted from heart rate and the actual QT interval. Smaller RSE values indicates better curve fitting. Ideally, after correction, the correlation between QTc and heart rate is zero, such that QTc is invariant of heart rate. For model 1, to calculate QTc-HR correlation we used the derived formula $QTc=QT/(60/HR)^{0.47}$, since the fitted parameter α was 0.47 for the first model.

Table 3. Regression models and QTc-HR correlation for the four QT correction methods

Regression model	α	β	RSE	QTc-HR correlation
1. $QT=\beta\times(60/HR)^{\alpha}$	0.47	412	14.9	-0.02
2. $QT=\beta\times(60/HR)^{1/2}$	-	417	15.1	0.16
3. $QT=\beta\times(60/HR)^{1/3}$	-	395	18.7	-0.62
4. $QT=\alpha\times(60/HR)+\beta$	236	181	15.3	-0.70
5. $QT=\alpha\times(HR/60)+\beta$	-98	496	16.5	0.17

Among the four correction methods, the Bazett method achieves the smallest RSE indicating that this method fits the curvilinear QT-HR relation more precisely than the Fridericia, Framingham and Hodges methods. The Bazett method also presents the smallest QTc-HR correlation coefficient (absolute value).

Model 1 fits even more precisely than the Bazett method for this dataset. However, it is likely that when applied to other datasets, model 1 (α=0.47) might not perform as well due to risk of over-fitting with the current dataset. As may be expected, various authors have reported different values of exponent α to perform most optimally for their own specific datasets [6, 9].

As shown in Figure 2, age clearly affects the QT-HR distribution. Distribution of points (QT, HR) from the five age groups demonstrates a shift from the top-left to bottom-right as age increases. We also applied the regression modeling within the five age groups separately. The parameter α from model 1 are 0.53, 0.44, 0.39, 0.39 and 0.41 for age groups 0, 1-5, 6-10, 11-15 and 16-20 years, respectively. Among the four correction methods, the Bazett formula performs best in age groups 0 and 1-5 years in terms of RSE and QTc-HR correlation. In the remaining age groups, the Bazett formula underperforms slightly relative to one or more other methods. However, each of the other methods either 1) significantly underperforms in another specific age group, or 2) fails to demonstrate both superior RSE and superior QTc-HR correlation in any specific individual age group (data omitted due to space constraints).

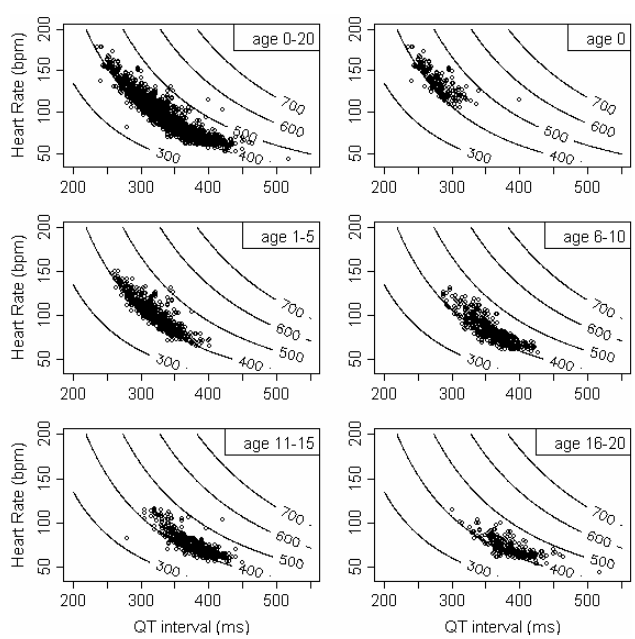

Figure 2. Scatter plots of QT versus HR by age groups on top of 3-D contour plot of the Bazett formula.

When considering a formula which can be applied to diverse pools of normal pediatric ECGs, α=0.5 (Bazett) may suggest a reasonable tradeoff between accuracy, generalizability and ease of use.

4. Discussion and conclusions

This study is the first to evaluate common QT interval correction methods in a set of normal pediatric resting ECGs spanning a wide age range. We determined that, among the four methods evaluated, the Bazett method fits the curvilinear relation between uncorrected QT interval and heart rate best, and also results in the least residual heart rate dependence after correction. The Bazett method yields more consistent readings across a wide range of ages and heart rates. To our knowledge, our study is also the first to suggest that the Bazett method may outperform other methods in a large sample set.

One limitation of this study is that we used retrospectively acquired normal ECGs, rather than prospectively acquired ECGs from healthy subjects. We unable to discern the original reason for obtaining the ECG. Demographic and clinical characteristics about our sampled ECG patient population are relatively coarse-grained and may limit generalizability. However, there are similarities between our findings and other reported investigations. First, the heart rate, QT interval, and QTc values in Table 2 are in accordance with those reported for other pediatric populations [10-11]. Second, our data mimics other datasets showing that QTc is significantly higher in females than males in the 16-20 year age group [12], and not different in age groups of infants [13] or younger children.

In conclusion, we find that use of the Bazett method in clinical evaluation of pediatric resting ECGs is supported by accuracy, simplicity and generalizability not yet surpassed by other available alternatives. Continued use of the Bazett method as a standard assists with making QTc values more consistently comparable across different institutions.

Acknowledgements

This study was supported by a grant from the Pew Charitable Trusts as part of the Clinical Genomics of Pediatric Cardiology Initiative at the Children's Hospital of Philadelphia. The investigative work was reviewed and approved by the Hospital's Institutional Review Board prior to its inception.

References

[1] Bazett HC: An analysis of the time relations of electrocardiograms. Heart 1920; 7:353-70
[2] Fridericia LS: Die Systolendaeur im elektrokardiogram bei normalen menchen und bei heizkranken. Acta Med Scand 1920; 53:469-86
[3] Sagie A, Larson MG, Goldberg RJ, et al. An improved method for adjusting the QT interval for heart rate (the Framingham study). Am J Cardiol 1992; 70:797-801
[4] Hodges M, Salerno D, Erlien D. Bazett's QT correction reviewed-Evidence that a linear QT correction for heart is better. J Am Coll Cardiol 1983; 12:694
[5] Lou S, Michler K, Johnston P, et al. A comparison of commonly used QT correction formulae: the effect of heart rate on the QTc of normal ECGs. J Electrocardiol 2004; 37:81-90
[6] Malik M, Farborm P, Batchvarov V, et al. Relation between QT and RR intervals is highly individual among healthy subjects: implications for heart rate correction of the QT interval. Heart 2002; 87:220-8
[7] Rautaharju PM, Zhang ZM. Linearly scaled, rate-invariant normal limits for QT interval: eight decades of incorrect application of power functions. J Cardiovasc Electrophysiol. 2002; 13:1211-1218
[8] Sadanaga T, Sadananag F, Yao H, et al. Heart rate dependent modification of the QTc cut-Off values can improve accurate evaluation of QT prolongation. Am J Cardiol. 2004; 39:772-775
[9] Wernicke JF, Faries D, Breitung R, Girod D. QT correction methods in children and adolescents. J Cardiovasc Electrophysiol. 2005; 16:76-81
[10] Rijnbeek PR, Witsenburg M, Schrama E, et al. New normal limits for the paediatric electrocardiogram. Eu Heart J. 2001; 22:702-711
[11] Schwartz PJ, Montemerlo M, Facchini M, et al. The QT interval throughout the first 6 months of life: a prospective study. Circulation. 1982; 66:496-501
[12] Rautaharju PM, Zhou SH, Wong S, et al. Sex differences in the evolution of the electrocardiographic QT interval with age. Can J Cardiol. 1992; 8:690-695
[13] Stramba-Badiale M, Spagnolo D, Bosi G and Schwartz PJ on behalf of the MISNES Investigators. Are gender differences in QTc present at birth? Am J Cardiol. 1995; 75:1277-1278

Address for correspondence

Geoffrey L. Bird
The Children's Hospital of Philadelphia
324 South 34th Street
Philadelphia, PA 19104, USA
bird@email.chop.edu