A new physiological method for heart rate correction of the QT interval

P Davey

Abstract

Aim—To reassess QT interval rate correction.

Background—The QT interval is strongly and inversely related to heart rate. To compare QT intervals between different subjects with different heart rates requires the application of a QT interval rate correction formula. To date these formulae have inappropriately assumed a fixed relation between QT interval and heart rate. An alternative method of QT interval rate correction that makes no assumptions about the QT interval–heart rate relation is needed.

Proposal—A QT heart rate correction method should maintain or accentuate biological QT interval variability, should totally remove the dependence of the rate corrected QT interval on heart rate, and should be applicable over a wide range of conditions with a wide range of different autonomic states.

Methods—QT intervals were obtained at rest and during exercise from subjects expected to have different QT intervals and different QT interval–heart rate relations. A linear regression line was obtained from the exercise test data, and the QT interval at a notional heart rate of 60 and 0 beats/min, termed the QT<sub>60</sub> interval, and the QT y intercept obtained by back calculation.

Results—QT<sub>60</sub> and QT y intercept values were prolonged in heart failure compared with either left ventricular hypertrophy or controls. There was no relation between heart rate and either QT<sub>60</sub> or QT y intercept.

Conclusions—This new physiologically based method of correcting QT interval for heart rate removes the dependence of the corrected QT interval on heart rate, and maintains biological differences.

(Heart 1999;82:183–186)

Keywords: QT interval; heart rate correction

The QT interval is increasingly often measured, partly to assess proarrhythmia in clinical practice, partly to determine the cardiac toxicity of non-cardiac drugs, and partly in the assessment of new antiarrhythmic agents. As heart rate has a powerful influence on the duration of the QT interval, to compare the QT interval from different subjects with different heart rates the QT interval needs to be heart rate corrected to a notional and identical heart rate. Various QT interval heart rate correction formulae have been proposed.1–9 There are two basic tests of the validity of the QT interval rate correction formulae. These tests are first, that the dependence of QT interval on heart rate should be totally removed by the application of the rate correction formula, and second, that the QT rate correction formulae should maintain or accentuate genuine biological differences in the QT interval between subjects. The formulae proposed to date have not been totally successful, principally in that corrected QT intervals still show rate dependence. Thus a new approach to QT interval rate correction is needed.

The basic assumption of rate correction formulae is that there is a fixed relation between QT interval and heart rate—that is, knowledge of the QT interval at one heart rate automatically allows one to correct the QT interval to all other heart rates. Thus individuals with the same QT interval and the same heart rate will all have the same rate corrected QT interval. These formulae therefore assume that the heart rate adaptation of the QT interval is the same in all individuals. However, it is known that QT interval rate adaptation can be influenced by disease and by drug treatment, and furthermore it is likely that even in normal subjects there will be variability within the normal range of QT interval rate adaptation.10–23 Thus it seems unlikely that an approach to the problem of QT interval rate adaptation that assumes a fixed QT interval to heart rate relation will be appropriate. Given this, it seems more appropriate that in correcting the QT interval for heart rate one should obtain the QT interval to heart rate relation for each and every subject, and use this relation to obtain a QT interval at a notional reference heart rate, for example at 60 beats/min. This approach would then allow one to make heart rate correction without having to make any assumptions about the QT–heart rate relation. The validity of this approach can be tested—first, by determining if this approach removes the dependence of QT interval on heart rate, and second, by determining if biological differences in the QT interval are maintained.

Hypothesis

A new heart rate to QT interval correction method should possess the following fundamental properties: it should maintain or accentuate biological QT interval variability; it should totally remove the dependence of the rate corrected QT interval on heart rate; and it should be applicable over a wide range of conditions with a wide range of differing autonomic states.
Table 1 Patient characteristics

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Hypertrophy</th>
<th>Heart failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>16</td>
<td>16</td>
<td>34</td>
</tr>
<tr>
<td>Ischaemic heart disease</td>
<td>10 (62%)</td>
<td>1 (6%)†</td>
<td>19 (56%)‡</td>
</tr>
<tr>
<td>Valvular heart disease</td>
<td>0</td>
<td>4 (25%)*</td>
<td>2 (6%)</td>
</tr>
<tr>
<td>LVIDsystole (mm)</td>
<td>47 (1)</td>
<td>56 (4)</td>
<td>63 (2)*</td>
</tr>
<tr>
<td>LVIDdiastole (mm)</td>
<td>29 (2)</td>
<td>35 (4)</td>
<td>51 (2)*</td>
</tr>
<tr>
<td>Fractional shortening</td>
<td>0.36 (0.03)</td>
<td>0.39 (0.02)</td>
<td>0.21 (0.02)‡</td>
</tr>
<tr>
<td>LV mass (g)</td>
<td>198 (15)</td>
<td>420 (48)*</td>
<td>403 (14)*</td>
</tr>
<tr>
<td>HRrest (beats/min)</td>
<td>74 (3)</td>
<td>68 (4)</td>
<td>86 (5)*†</td>
</tr>
<tr>
<td>QTc (ms)</td>
<td>381 (6)</td>
<td>399 (9)</td>
<td>400 (11)</td>
</tr>
<tr>
<td>QTc peak (ms)</td>
<td>421 (6)</td>
<td>420 (6)</td>
<td>471 (10)*‡</td>
</tr>
<tr>
<td>HRest (beats/min)</td>
<td>141 (5)</td>
<td>131 (7)</td>
<td>131 (4)</td>
</tr>
<tr>
<td>QT peak (ms)</td>
<td>281 (7)</td>
<td>296 (11)</td>
<td>303 (10)</td>
</tr>
</tbody>
</table>

Values are mean (SEM) unless stated.

*p < 0.05 v control; †p < 0.05 v hypertrophy.
HR, heart rate; LV, left ventricular; LVID, left ventricular internal dimension.
Heart rate correction of the QT interval

The relation between QT interval and RR interval is linear. Two propose linear QT–heart rate relations, and in one the formula is derived from fundamental thermodynamic principles. Other formulae propose more complex relations between QT interval and heart rate. There are many formulae accept that there are important differences based on sex or age between individuals in the dependence of the QT interval on heart rate. None of the proposed formulae, however, incorporate differences based on disease status. As many cardiac diseases alter both the QT interval and the function of the autonomic nervous system, it would not be surprising if the rate dependence of the QT interval was altered in heart disease. It is in just these individuals with diseased hearts that one wishes to measure the QT interval. Thus in order to use a formula to correct the QT interval in patients with heart disease, one will need a very large dataset that incorporates the effect of the heart disease as well as the effects of cardioactive drugs on the rate dependence of the QT interval. This approach may not be practical.

An alternative approach is to determine the rate dependence of the QT interval for each individual, and use this to correct the QT interval to a notional heart rate. The data presented here show that using individualised heart rate dependence for the QT interval allows one to correct the QT interval for the effects of heart rate. Furthermore, the results show that using exercise test data to correct the QT interval individually to a nominal heart rate of 60 beats/min satisfies the two important criteria of a QT–heart rate correction algorithm, which are that the rate correction method should totally remove the dependence of QT interval on heart rate but at the same time maintain biological differences.

Given that it is physiologically based—and therefore makes no assumptions about the nature of the relation between QT interval and heart rate—and that it completely removes all dependence on heart rate while at the same time maintaining biological diversity, this method of QT interval–heart rate correction is superior to previous methods that have assumed a fixed relation between QT interval and heart rate, as those methods failed to remove the relation between corrected QT interval and heart rate. Because Bazett’s method of correcting for heart rate consistently overcorrected the QT interval at high heart rates, and because high resting heart rates are found in heart failure, there has up to now been some concern that prolongation of the QTc interval found in heart failure is not the result of a genuine prolongation of repolarisation but is rather an artefact of the rate correction formulae. The findings from this study indicate that there is genuine prolongation of repolarisation in heart failure. This finding may aid our understanding of arrhythmogenesis in heart failure. Lethal ventricular arrhythmias are particularly prevalent in heart failure, as is QTc interval prolongation. It remains to be seen whether QTc prolongation relates to arrhythmogenesis, but if it does, this may suggest that

Table 2 QT60 data

<table>
<thead>
<tr>
<th>Control</th>
<th>Hypertrophy</th>
<th>Heart failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>QT60 (ms)</td>
<td>404 (5)</td>
<td>411 (6)</td>
</tr>
<tr>
<td>QT y intercept (ms)</td>
<td>497 (7)</td>
<td>511 (12)</td>
</tr>
</tbody>
</table>

Values are mean (SEM).

*p < 0.05 vs control; †p < 0.05 vs hypertrophy.

Figure 2 QT and QTc data. Data for the entire population are plotted here, before and after rate correction using Bazett’s method. Each point represents the mean of the QT intervals for one subject while at rest. Linear regression analysis shows that uncorrected QT interval is significantly related to heart rate, with \( r^2 = 0.34 \) (p = 0.0001). After rate correction, however, there is still a relation with heart rate which, while weaker than that between the uncorrected QT interval and heart rate, is still significant, with \( r^2 = 0.10 \) (p = 0.02).

Figure 3 QT60 plotted against heart rate. There was no relation between QT60 and heart rate, with \( r^2 = 0.002 \) (p = 0.74).
an important component of sudden cardiac death in heart failure relates to mechanisms dependent upon prolonged repolarisation, and these particularly include repetitive afterdepolarisations.24–26

Though for reasons of convention I arbitrarily chose to correct the QT interval back to a notional heart rate of 60 beats/min, the fact that the QTy-intercept—which is when the notional heart rate was 0 beats/min—showed no relation with heart rate and was prolonged in heart failure meant that we could have chosen any value of heart rate between 0 and 60 beats/min for the notional heart rate corrected QT interval.

**IMPLICATIONS**

This study may have important implications for future QT interval analysis, in particular of data obtained from 24 hour Holter ambulatory recorders. Computer software that can determine QT interval from Holter recorders is becoming increasingly widespread. This approach to QT interval analysis may have many advantages over more conventional ways of measuring the QT interval. Not only should this approach minimise variability in the measurement of the QT interval, which may allow the QT interval to be used more reliably in predicting sudden cardiac death, but it will also allow us to analyse data in novel ways. With the large number of QT–heart rate point pairs one can obtain—approximately 100 000 QT intervals in 24 hours—one could calculate the QT–heart rate relation on, say, an hour to hour basis over the 24 hours, and use this to calculate an hourly QT60 interval, which can then be tested against variables of interest. This looks like a promising approach to correcting the QT interval for heart rate without the need to make any assumptions about the relation between QT interval and heart rate; however, this physiologically based method of correction of the QT interval will need to be validated for day to day exercise, as opposed to laboratory based exercise tests, before it can be held to be generally applicable.

**LIMITATIONS**

This method of correcting the QT interval for the effects of heart rate requires a number of measurements of QT interval at different heart rates, which in this study were obtained from an exercise test. This is clearly a time consuming exercise, and it may be that this method will be principally limited to the research field. However, QT interval measurement is of most interest in patients with heart disease, many of whom undergo exercise testing. With the increasing use of computer based QT interval analysis, it may be relatively easy to incorporate this method of analysis into future exercise machines.

The department receives a grant from the British Heart Foundation.

9 Kovacs SJ. The duration of the QT interval as a function of heart rate: a derivation based on physical principles and a comparison to measured values. Am J Heart 1985;110:872–8.
A new physiological method for heart rate correction of the QT interval

P Davey

Heart 1999 82: 183-186
doi: 10.1136/hrt.82.2.183

Updated information and services can be found at:
http://heart.bmj.com/content/82/2/183

These include:

References
This article cites 26 articles, 7 of which you can access for free at:
http://heart.bmj.com/content/82/2/183#BIBL

Email alerting service
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Topic Collections
Articles on similar topics can be found in the following collections

Drugs: cardiovascular system (8842)

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/