Editorial Comment

Time for Yet Another QT Correction Algorithm? Bazett and Beyond*

MICHAEL R. FRANZ, MD, PhD, FACC
Washington, D.C.

Since Bazett's original publication in 1920 (1), a spate of new QT interval correction algorithms have appeared (2). Many of these proposals are based on a larger number of patients, use more sophisticated statistical analyses techniques and demonstrate a better fit to actual data than the Bazett formula. Why, then, do we ask, does the Bazett QT interval correction algorithm still prevail in everyday practice? One reason for its popularity may be its simplicity of use. But electrocardiographic (ECG) rulers with nonograms and computerized ECG machines could easily implement more complex correction formulas. Is it because cardiology in this one area is more conservative than in other areas where progress is being embraced rapidly? Or is it because no really convincing solution has yet been offered to the enigma of the QT interval and the effect that heart rate has on it? I believe that the last argument is mostly true. I believe that the adoption of newer and better algorithms has been slow because a true appreciation of the factors that govern normal and abnormal repolarization has not yet appeared.

The Bazett formula has apparent flaws. Because of its square root equation, the Bazett formula predicts an ever-growing QT prolongation with slowing heart rates and an insufficient shortening toward faster heart rates. Both of these mathematical predictions, shared by the Bazett formula as well as by other uniform rate-correcting algorithms, are in contrast with experimental and clinical observations that duration of myocardial repolarization would increase without an upper limit. This is contradicted by experimental and clinical data that demonstrated that the action potential duration attains a finite duration or limit regardless of the degree of heart rate slowing (3).

Present study. In this issue of the Journal, Karjalainen et al. (6) propose yet another approach to correct the QT interval on the basis of the prevailing heart rate. Their QT correction algorithm is novel in that they have used three separate linear regression functions to correct the QT interval for heart rate, each function describing the relation between heart rate and the QT interval for a different range of heart rates. Earlier contenders for the Bazett formula include the Fridericia formula, which is based on a cubic root equation (2), and the more recent Framingham study, which assumes linearity (7). These, like all previously published QT correction algorithms, whether one-variable equations or complex multivariable equations, have in common that a single function is assumed to be valid over the entire range of heart rates. This, however, makes them more suitable at one heart rate range than at another. For instance, Fridericia's cubic root formula (QT_F = QT/RR^{1/3}) gives better correction at low heart rates than at high heart rates.

The linear regression equation of the Framingham Study (QT_{LR} = QT + 0.154(1 - RR)) is reliable at normal heart rates but fails at low and high heart rates. Bazett's formula (QT_e = QT/RR^{1/2}) performs poorest at all heart rate subranges. The Karjalainen et al. formula appears to be superior by direct comparison with those three equations, at least in their study population of healthy young men.

What I find attractive about the Karjalainen et al. data interpretation is that basic electrophysiologic data also have emphasized a linear relation between the cycle length and duration of myocardial repolarization. For instance, a study of monophasic action potential durations recorded from the human right ventricular endocardium during steady state pacing at cycle lengths ranging from 350 to 1,300 ms exhibited a closely linear correlation with cycle length over the range 350 to 700 ms and at cycle lengths >800 ms, flattened into a plateau (5). The linear correlation phase and the plateau phase were connected by a transition phase. Hence, the rate dependence of myocardial repolarization at the cellular level also is best described by three separate yet overlapping functions.

Is there a physiologic explanation for different regression coefficients for different heart rate ranges? Possibly. It has been shown that the action potential duration depends in part on the electrical diastolic interval preceding the beat in question. This factor is represented graphically by the electrical restitution curve, which describes the recovery, or gradual lengthening of the action potential duration from the earliest premature beat to the longest coupling interval achievable (5). At fast heart rate, the diastolic interval is shorter than the action potential duration. This leads to

*Editorials published in Journal of the American College of Cardiology reflect the views of the authors and do not necessarily represent the views of JACC or the American College of Cardiology.

From the Divisions of Cardiology and Clinical Pharmacology, Georgetown University Medical School and Cardiology Division, Veterans Administration Medical Center, Washington, D.C.

Manuscript received March 1, 1994; revised manuscript received March 22, 1994; accepted March 24, 1994.

Address for correspondence: Dr. Michael R. Franz, Cardiology Division, Veterans Administration Medical Center, 30 Irving Street, NW, Washington, D.C. 20422.

©1994 by the American College of Cardiology

0735-1097/94$7.00
incomplete recovery of repolarization processes from one beat to the next and helps shorten the action potential duration further. There is a limit to action potential duration shortening, however, as exemplified by intracardiac recordings made during rapid ventricular tachycardia or ventricular fibrillation (3,4). Here, the cycle length is so short that consecutive action potentials follow each other with no or very brief diastolic intervals (3). Hence, QT correction for cycle length has reached its lower limit. On the other hand, at slow heart rates, the diastolic interval is much longer than the action potential duration. For instance, at a heart rate of 60 beats/min or a cycle length of 1,000 ms, the action potential duration may be 300 ms long and the diastolic interval 700 ms long. According to the electrical restitution curve, action potential duration recovery is complete at such long diastolic intervals, and further cycle length shortening will not produce further action potential duration shortening. Thus, the action potential duration versus cycle length relation has reached a final plateau (i.e., its upper limit). On the basis of these observations, for which ionic mechanisms have been proposed (5), the cycle length/QT relation is not a continuous function nor an unlimited one. Rather, there are finite minima and maxima, and the weight that the cycle length has in affecting the QT interval changes over the range between these minima and maxima.

Limitations of QT correction. A shortcoming of all QT correction algorithms proposed to date is that they do not take into account the effect of the myocardial heart rate "memory." Neither the cardiac action potential duration nor the resulting QT interval adjust instantaneously to the immediately preceding cycle length but follow a biphasic time course of adaptation. After a sudden change in heart rate, up to 3 min may be required before the action potential duration reaches a steady state for the new heart rate (5). Therefore, the curve relating the action potential duration (or QT interval) to the cycle length is steeper when it is determined during steady state conditions than when it is analyzed shortly after a cycle length change (5). In patients with the long QT syndrome, the adaptation process of the myocardium to heart rate changes itself may be altered. The use of QT rate correction algorithms derived from normal patients may mask rather than expose the abnormal repolarization response to heart rate in the long QT syndrome.

Another limitation of QT correction algorithms is that they do not take into account the modulating effects of the autonomous nervous system. Sympathetic influences are known to shorten ventricular repolarization independent of the concomitant effect on heart rate (8,9). As pointed out by Karjalainen et al. (6), this may be one of the reasons why QT measurements in rest ECGs do not correlate well with QT measurements in Holter recordings. Holter recordings within the same subject at low and high heart rates reflect different degrees of sympathetic tone and therefore may yield different QT intervals than population data obtained from different subjects with different rest heart rates. Further, autonomic influences modify both action potential duration shortening or lengthening in the ventricle and may do so disparately among different regions of the ventricle, depending on the proportionality between sympathetic/parasympathetic innervation and on the degree with which different ventricular myocardial regions respond to such autonomic stimuli (9).

Does QT correction serve its primary purpose? Why is an accurate and meaningful assessment of the QT interval so important? The primary importance lies in the fact that an abnormally prolonged QT interval bears a risk for the patient to develop polymorphous ventricular tachycardia including classical torsade de pointes arrhythmias. The present study does not contribute to a better recognition of the upper limit of normal. The reason for this is the small sample size as well as the all-male population.

After the disappointing results of the Cardiac Arrhythmia Suppression Trials (CAST), which implicated an increase in sudden cardiac death in patients treated with sodium-channel blocking drugs (class IC drugs), new hope for effective antiarrhythmic therapy has focused on class III drugs, which, if pure, prolong ventricular repolarization and do nothing else. However, with the exception of amiodarone, pharmacologic prolongation of repolarization is associated with the risk for polymorphous arrhythmias, similar to those seen in patients with the congenital long QT syndrome. If the desired antiarrhythmic effect of these class III agents is achieved by an increase in ventricular repolarization time, how can we know how much prolongation of the QT interval is sufficient and how much is dangerous? (10). Furthermore, how can we know that QT correction algorithms can guide us in predicting the beneficial versus the hazardous prolongation of the QT interval in patients who have different heart rates? This confusing issue is further confounded by the fact that most class III antiarrhythmic drugs exhibit reverse use dependence. This means that their action potential duration–prolonging effect diminishes with increasing heart rates and becomes greater toward slow heart rates. No QT correction algorithm has yet been proposed to solve this dilemma.

Other repolarization indexes. In patients with the long QT syndrome, both congenital and acquired, the abnormally prolonged QT interval and the arrhythmia propensity may be due to early afterdepolarizations rather than to a prolongation of the repolarization phase proper. The ECG representation of these early afterdepolarizations appears to be enhanced U waves rather than T wave prolongation (11). It is often difficult to discern the U wave from the T wave, especially in patients with long QT syndrome where there is often T-U wave fusion. Thus, QT correction algorithms, which do not take into account the U wave or include the U wave unknowingly for QT interval measurements, would ignore the existence of such an arrhythmogenic and potentially fatal repolarization abnormality.

The QT interval itself may not be the most decisive arrhythmogenic index found in ECG recordings. The QT interval is measured in the lead with the largest T wave.