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QT Interval: How to Measure It and What Is "Normal"

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Abnormally long and short QT intervals have been shown to be associated with an increased risk for life-threatening ventricular arrhythmias and sudden cardiac death. In recent years, various methods for QT-interval measurement have been developed, including individual-based corrections for repolarization duration, quantitative assessment of repolarization morphology, correction for repolarization dynamicity, and analysis of repolarization variability. However, these methods require computer-processed digital-signal analysis of electronically stored ECG data and have been used most frequently in the assessment of repolarization changes in drug trials. In the present review, we will focus on methods for clinically relevant visual and manual assessment of QT-interval duration from a 12-lead ECG, which can be utilized in day-to-day practice for the diagnosis of long QT syndrome (LQTS) and other repolarization disorders.

ECG Assessment

The 12-lead ECG is the most frequently used technique for obtaining the surface electrocardiographic signal for evaluation of ventricular repolarization. Manual ECG readings are performed using visual determinations ("eyeball"/caliper techniques), digitizing methods, and/or on-screen computerized methods. The accuracy of the automatic measurements of the corrected QT (QTc) interval is questionable in many cases and should be supplemented by manual reading. Inconsistency between manufacturers in terms of the algorithms used for calculation of the intervals is another problem in the interpretation of computerized readings. Some digitizing methods employ a digitizing pad, magnifying lamp, and pointing device to identify the beginning and end of the QT interval, with an accuracy level of 5 ms. A more technologically advanced option is to display digitally recorded ECGs on a computer screen, where they can be measured using computer-driven, on-screen calipers. This latter approach provides high-quality ECG data and is recommended at core laboratories performing centralized analyses of a large ECG database. Scanned paper-recorded ECGs can also be subjected to on-screen measurements.

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The accuracy levels of manual determination with a caliper is 20–40 ms. A standard 12-lead ECG tracing at 25 mm/s paper speed at 10 mm/mV amplitude is generally adequate for accurate measurement of QT-interval duration. Higher speeds (e.g., 50 mm/sec) may lead to distortion of low-amplitude waves such as U waves. The QT interval should be determined as a mean value derived from at least 3–5 cardiac cycles (heartbeats), and is measured from the beginning of the earliest onset of the QRS complex to the end of the T wave. The QT measurement should be made in leads II and V5 or V6, with the longest value being used. The main difficulty lies in identifying correctly the point where the descending limb of the T wave intersects the isoelectric line, particularly when there are T and U waves that are close together. We identify the end of the T wave when its descending limb returns to the TP baseline when it is not followed by a U wave (Fig. 1A) or if it is distinct from the following U wave (Fig. 1B). When T-wave deflections of equal or near-equal amplitude result in a biphasic T wave, the QT interval is measured to the time of final return to baseline (Fig. 1C). If a second low-amplitude repolarization wave interrupts the terminal portion of the T wave (Fig. 1D), it is difficult to determine whether the second deflection is a biphasic T wave or an early-occurring U wave. In such cases, it is best to record both the QT interval (T-wave offset measured as the nadir between the T and U wave) and the QTU interval (repolarization offset measured at the end of the second wave). In general, biphasic T waves are frequently present in multiple leads, whereas discrete and separate low-amplitude U waves are best seen in the lateral precordial leads. The end of the U wave is defined as the intersection point of the descending limb of the U wave and the isoelectric baseline. This method reflects accurately the real duration of ventricular repolarization, but it introduces a large degree of subjectivity, particularly when biphasic T waves are present or when large U waves interrupt the return of the T wave to the baseline. The method can be effectively applied for manual measurements, but is less suitable for computer analysis because it requires the definition of a given threshold for the amplitude below which T or U wave potentials return to baseline.

The QRS interval can be modified by several factors (such as bundle branch block, Class 1c antiarrhythmic drugs, or preexcitation); these changes in depolarization can alter repolarization in unexpected ways, and thus the QT interval may not be an accurate reflection of repolarization duration. In these patients, the measure of the JT from the S-wave offset to T-wave end may be used, but normal standards for the JT interval are not well established.

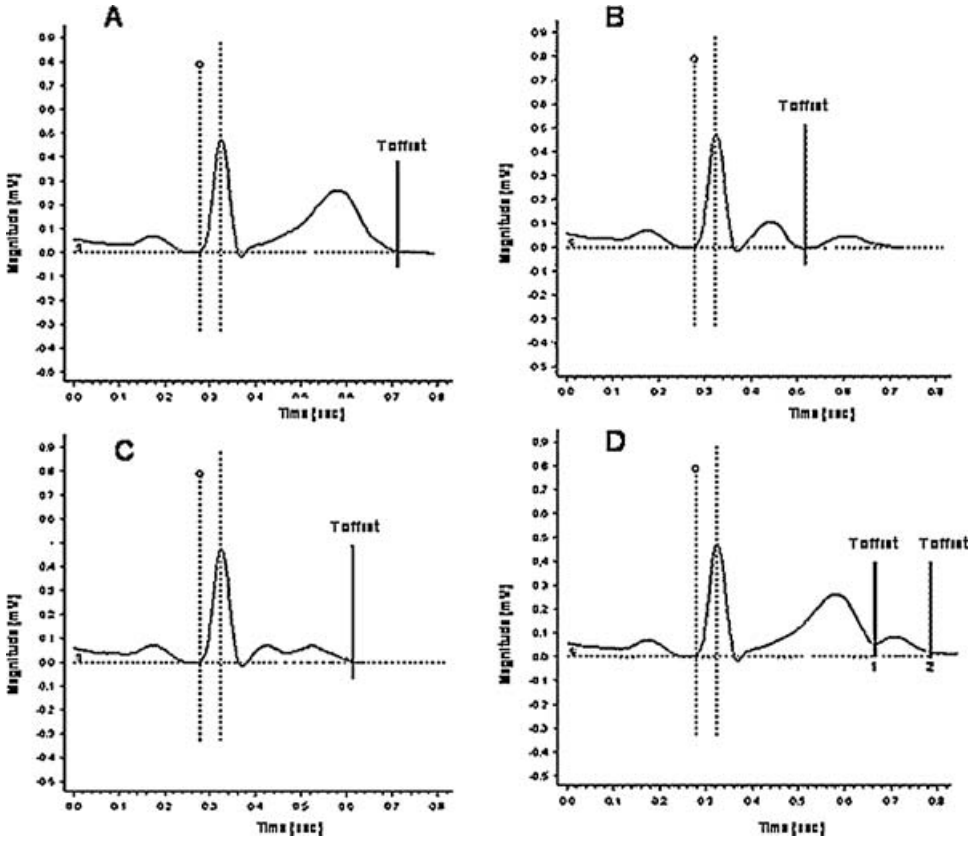

Figure 1. *(A) When the T-wave morphology is normal, the T-wave offset is identified when the descending limb returns to the TP baseline; (B) when the T wave is followed by a distinct U wave, the T-wave offset is identified when the descending limb of the T wave returns to the TP baseline before the onset of the U wave; (C) when the T wave is biphasic with T1 and T2 waves of similar amplitude, the T-wave offset is identified at the time when T2 returns to baseline; and (D) when a second low-amplitude repolarization wave interrupts the terminal portion of the larger T wave (? whether it should be categorized as T2 wave or a U wave), the T-wave offset should be measured both at the nadir of the two waves (1) and at the final return to baseline (2).*

Adjustment for Heart Rate

The time–duration intervals are influenced by heart rate (R–R cycle length), so heart rate correction is required in the analysis of repolarization duration. Various heart rate correction formulae have been developed in order to determine whether the QT interval is prolonged in comparison to its predicted value at a reference heart rate of 60 beats/min (i.e., an RR interval of 1.0 second). These formulae have been derived mainly from resting ECGs, and therefore require a stable sinus rhythm without sudden changes in the RR interval. Exponential, logarithmic, and linear formulae have been used[1] (Table 1). To assess the performance of a particular heart rate correction formula, the correlation between the corrected QT (QTc) intervals calculated using the formula and the RR intervals can be assessed. If it differs from zero, as is the case

TABLE 1

QT-Heart Rate Correction Formulas[1]

Method	Formula	Comment
Exponential		
Bazett	$QTc = QT/RR^{1/2}$	Widely used; may give erroneous results at both slow and fast heart rates
Fridericia	$QTc = QT/RR^{1/3}$	Widely used; may give more consistent results at fast heart rates
Linear		
Framingham	$QTc = QT + 0.154(1\text{-}RR)$	May have more uniform rate correction over a wide range of heart rates
Hodges	$QTc = QT + 1.75(HR\text{-}60)$	
Rautaharju		May have more uniform rate correction over a wide range of heart rates
Females and males <15 and >50 years	$QTI = (QT[HR + 100])/656$	
Males 15–50 years	$QTI = 100(QT)/([656/(1 + 0.01HR]) + 0.4–25)$	
Logarithmic		
Ashman	$QT = K1 \times \log(10 \times [RR + K2])$	At low heart rates, the values are too low
Adult men	$K2 = 0.07$, and $K1 = 0.380$	
Adult women	$K2 = 0.07$, and $K1 = 0.390$	

with most of the above-described formulae, the correction formula is not truly successful. We most commonly correct the interval by using Bazett's square root formula. QTc is equal to QT interval in seconds divided by the square root of the preceding RR interval in seconds. When heart rate is particularly fast or slow, the Bazett's formula may overcorrect or undercorrect, respectively, but it remains the standard for clinical use. The cube root Fridericia formula has the same limitations at slow heart rates, but is considered to reflect a more accurate correction factor in subjects with tachycardia. Linear formulae may have more uniform correction over a wide range of heart rate. The most commonly used linear formula derives from the Framingham study. The latter formulae may give QT values that are too low at slow heart rates. There is no general consensus on the best formula to be utilized in clinical practice. Of note, in resting conditions with heart rates in the 60–90 beats/min range, most formulae provide almost equivalent results for the diagnosis of QT prolongation. Even if the rate dependence of the QT interval is probably best described by an exponential relation, in the normal heart rate range the QT–RR relation is approximately linear.

Heart Rate Correction in Patients with Sinus Arrhythmias

If a stable sinus rhythm cannot be obtained in a patient, more advanced methods evaluating repolarization dynamicity may be required. The QT interval adapts to heart rate changes with a delay known as QT hysteresis or QT lag. When the change in the heart rate persists for several minutes, the QT lag is visible on the trend of QT and RR intervals. The QT adapts more slowly to decelerations than to accelerations of the heart rate. The plot of QT versus RR intervals during dynamic adaptation of repolarization to heart rate changes forms a loop known as hysteresis. QT–RR hysteresis pattern is highly individual and, therefore, methods that take into account individual profiles are required.

Normal Values of the QT Interval (12-Lead ECG)

Bazett's formula has been more frequently used in medical publications than Fridericia's formula. Therefore, most reported criteria for normal and abnormal values for QTc are derived from Bazett's formula. Our research group has utilized digitized data file for QT- and RR-interval measurements on 581 healthy individuals: 158 children aged 1–15 years (80 boys and 78 girls) and 423 adults aged 16-81 years (223 men and 200 women). Using this data set, we evaluated the range of Bazett QTc values by age and gender. The QTc values were stable for children, with no gender difference, while there was a significant difference between adult men and women in this healthy population.[2]

TABLE 2

Suggested Bazett-Corrected QTc Values for Diagnosing QT Prolongation

Rating	1–15 years (msec)	Adult Male (msec)	Adult Female (msec)
Normal	<440	<430	<450
Borderline	440–460	430–450	450–470
Prolonged	>460	>450	>470

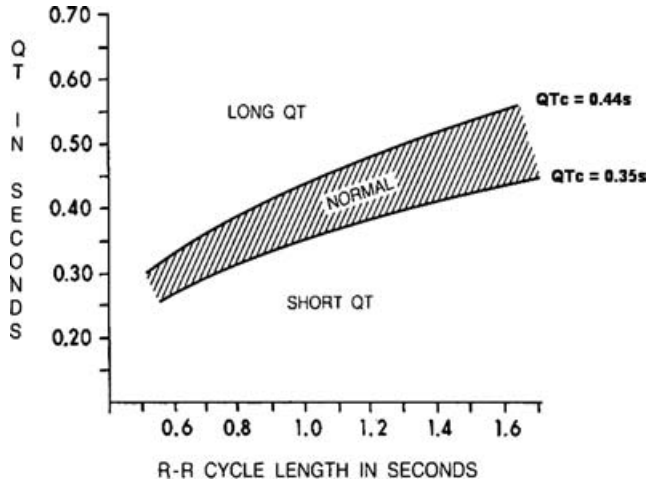

Figure 2. *Lower and upper limits of QT interval for different RR cycle lengths based on QT-interval measurements in normal healthy subjects.*

A suggested three-level classification based on this analysis is presented in Table 2.

A simple graphical display of lower and upper limits of QT interval for different RR cycle lengths based on population studies has been developed in our laboratory (Fig. 2). The data can be used by clinicians for reference purposes.

Repolarization Morphology

Recent advances have been made in quantitating repolarization using such measurements as the symmetry of the T wave, T-wave area, or the interval between the end of the S wave and the maximum amplitude of the T wave. However, quantitative analysis of the T-wave shape and pattern requires computer software and electronically stored ECG data.

The morphology or configuration of repolarization can be described from visual inspection of the T wave and placed into prespecified categories. In our assessment of ventricular repolarization, we incorporate this information into the data obtained from QT-interval duration measurement. Distinctive T-wave patterns have been observed in patients with each of the three major LQTS genotypes (Fig. 3).[3] In LQT1 a single, smooth, broad-based T wave is common, as well as a late-onset normal-appearing T wave; in LQT2, bifid T waves are a hallmark ECG feature; in LQT3, the T waves are typically late-onset, prominent, and usually peaked.

Other ECG Recording Techniques

Holter and exercise testing have also been used to evaluate the QT interval. Holter monitoring is not sufficiently well standardized to serve in the primary assessment for ventricular repolarization analysis. However, we sometimes employ this method for the detection of extreme QT-interval events that occur infrequently during the day. Since QT intervals measured using the Holter methodology do not correspond quantitatively to those for standard ECGs, data obtained from the two methodologies are not suitable for direct comparison. Exercise testing with a standard activity protocol can be used for evaluation of QT prolongation during exercise and recovery periods. Intermittent 12-lead ECGs or

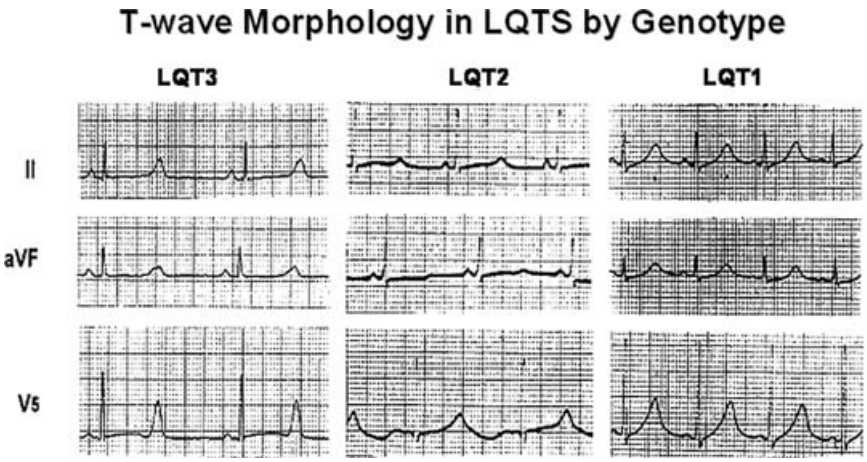

Figure 3. *Specific LQTS T-wave patterns: broad-based T-wave pattern in LQT1, bifid T waves in LQT2, and late-onset peaked/biphasic T waves in LQT3. Reprinted with permission from Moss AJ, Zareba W, Benhorin J, et al. Circulation 1995; 92:2929-2934.*

continuous multichannnel ECG recordings can be used. However, the adaptation of QT-interval duration to heart rate is not instantaneous, and substantial errors may be introduced if nonstationary episodes are analyzed.

Recent analysis from the International LQTS Registry demonstrates that there is individual subject variability in QTc duration on repeat ECGs during long-term follow-up extending over several years. Therefore, we suggest that several ECGs recorded over time should be more useful in identifying subjects with abnormally long or short QT intervals than simply one baseline ECG recording.

Conclusions and Recommendations

The simple measurement of the QT interval is valuable for the diagnosis of abnormal QTc intervals. However, the routine measurement of the QT interval requires the use of uniform criteria for the determination of T-wave offset (especially when there is partial superimposition of the T and U wave), adjustment for heart rate, and T-wave morphology.

In a recent study,[4] correct classification of QT intervals (either "long" or "normal") using only manually measured QT and RR intervals was achieved by 96% of QT experts and 62% of arrhythmia experts, but by only <25% of cardiologists and noncardiologists. Clearly, experience and training play an important role in the accurate measurement of the QTc interval.

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