The assessment of the QT interval

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Abstract

QT measurement should be included as part of the systematic interpretation of the electrocardiogram (ECG). Accurate measurement and interpretation of the QT interval will help to identify potentially fatal Long QT Syndromes (LQTS). The assessment of the QT interval, correction of the QT and the guidelines relating to it, are complex. This article discusses the importance of this element of the ECG and offers practical advice on QT assessment based upon a review of the relevant literature.

Key Words

QT, QTc, ECG, Long QT Syndrome (LQTS)

Introduction

The measurement and assessment of the QT interval, despite being an essential element of ECG interpretation, is not straightforward; in fact, it is surprisingly complex and fraught with pitfalls. Authoritative authors such as Goldenberg and Moss (2004) and bodies such as the American College of Cardiology (ACC), American Heart Association (AHA) and European Society of Cardiology (ESC) (2006) offer guidance which is challenging to apply owing to the complex nature of both QT measurement and LQTS itself. While some of the recommendations for practice are based on evidence, some are not. We will attempt to review the various current guidelines, pointing out the

flaws and difficulties where they are evident, and arrive at some sensible recommendations that can be used in practice.

The QT interval (Figure 1) represents the total time of ventricular depolarization and repolarization and is measured from the beginning of the QRS to the end of the T wave.

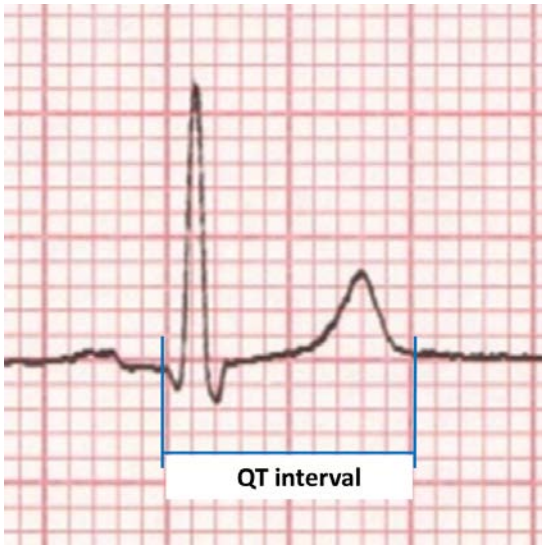

Figure 1: The QT interval

Accurate assessment of the QT interval is essential to identify LQTS, which has an estimated prevalence of between 1 in 2000 and 1 in 2,500 (Schwartz et al, 2009; Hayashi et al, 2009). However, despite the importance of identifying this often life threatening syndrome, the condition often goes undiagnosed. The first presentation in young people can be syncope or cardiac arrest associated with exercise or loud noises, or during sleep, and unless LQTS is considered, these symptoms may be mistakenly attributed to epileptic seizures (MacCormick et al, 2009; Kouzam and Kouzam, 2009 and the report by the All Party Parliamentary Group on Epilepsy, 2007). Taggart et al (2007), however, highlight the possible negative consequences for the patient resulting from over-diagnosis of LQTS. Accurate identification of abnormal QT length through systematic ECG interpretation, followed by

robust risk stratification, will help people with LQTS gain the appropriate treatment to avoid preventable sudden death and prevent a mistaken diagnosis of LQTS in those who do not have it.

In LQTS the increased risk of syncope or sudden death arises as a result of ion channel abnormalities that result in prolongation of the action potential with delayed repolarization. Early afterdepolarisations may cause tachyarrhythmia's, the most dangerous being torsades de pointes, a type of polymorphic ventricular tachycardia that frequently progresses to ventricular fibrillation (Fogoros, 2012).

LQTS may be inherited or acquired. Inherited (or congenital) LQTS is an autosomal dominant hereditary condition (meaning the children of a carrier of the gene mutation have a 50% chance of inheriting the syndrome). Acquired LQTS may be due to drugs or metabolic disturbances arising from conditions such as anorexia nervosa or hypothermia (Khan et al, 2010) and proven alcoholic liver disease (ACC/AHA/ ESC, 2006).

Correction of QT for heart rate

The QT interval is inversely related to the heart rate. In other words, the higher the heart rate, the shorter is the QT interval. This means that after the QT interval has been measured it must be mathematically corrected for the heart rate. The reference heart rate for QT measurement is 60bpm, so the aim of the mathematical correction is to calculate the QT interval that would have been obtained if it had been measured at a heart rate of 60bpm. The corrected QT is referred to as the QTc. Many QT correction formulas have been developed over the years (Luo et al, 2004); some of them are illustrated in Table 1. A quick alternative method to assess whether the QT is normal is simply to check that it is less than half the preceding RR interval (Garcia and Holtz, 2001).

Bazett	1920	QTc = QT divided by the square root of the previous R-R
Fridericia	1920	QTc = QT divided by the cube root of the

		previous R-R
Hodges	1983	QTc = QT+1.75(HR-60)
Framingham	1992	QTc = QT+0.154(1-RR)

Table 1: some commonly used QT correction formulas

The most commonly used formula was devised by Bazett nearly 100 years ago (Bazett, 1920) but its use has been criticised on the grounds that its correction of the QT interval is not accurate, particularly at very low and high heart rates. The American Heart Association (AHA) recommends that Bazett's formula not be used (Rautaharju et al, 2009), although, perhaps unhelpfully, it does not recommend a particular alternative. In contrast, a multi-national group that issued guidelines earlier this year for the diagnosis of heart disease in athletes (Drezner et al, 2013) recommended that Bazett's formula should be used. Despite its imperfections, we believe that Bazett's formula should remain the standard. Nearly all the information we have about the risk of sudden cardiac death in relation to QTc interval comes from studies in which Bazett's formula was applied to the measured QT, so it makes little sense to abandon Bazett now for an alternative.

In patients with an irregular heart rhythm, such atrial fibrillation (AF) or atrial flutter with varying block, there is no consensus on how the QT interval should be assessed. A study of 50 patients with AF found that the relationship between heart rate and QT interval was complex, and though the investigators found that AF appears to be associated with prolongation of the QT compared with the same heart rate in sinus rhythm, they concluded that it was not possible to correct the QT for the heart rate by applying a simple formula such as Bazett's (Pai and Rawles, 1989). Fortunately, because AF is rare in children and young adults, this is unlikely to present a significant problem in the diagnosis of congenital LQTS.

Which lead (s) should be used for the measurement of QT interval?

Most clinical studies have used lead II or, if the T wave in lead II is indistinct, leads I or III for the measurement of the QT. Others have used V5 as an alternative to lead II (Vetter, 2007) when that is not suitable. The current AHA recommendation (Rautaharju et al, 2009) is to display and view all 12 leads of ECG simultaneously, as in figure 2, and measure the QT interval from the earliest QRS onset to the latest T wave end. This will produce a QT interval that is longer than that which would be measured in any single lead. Not only is this method frequently impracticable, because all 12 leads of an ECG are rarely displayed simultaneously, it has not been used by any of the most important large-scale studies from which we have derived our clinical knowledge of long QT syndrome. As a more practical alternative, where a simultaneous 12-lead display is not available, AHA recommends that the QT interval be measured in all 12 leads and the longest quoted. The original source of this recommendation is a paper written over 60 years ago (Lepeschkin and Surawicz, 1952), several years before long QT syndrome was first described, and it is an approach that has never gained wide acceptance in practice.

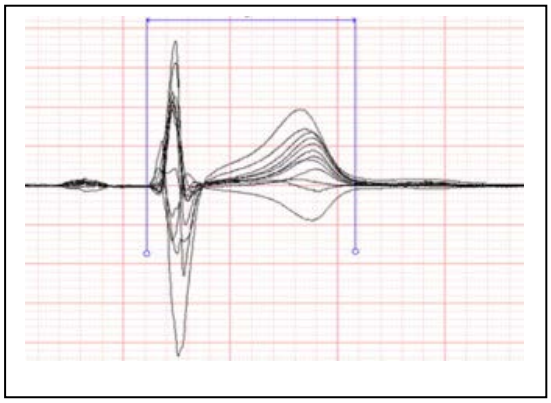

Figure 2: QT interval from 12 simultaneous superimposed leads: image from Vaibhav et al (2011)

The most important feature of the lead selected for measurement of the QT is that the end of the T wave be clearly visible. We suggest that lead II be used if the T wave end is distinct; otherwise, lead I, III or V5 should be used, according to which allows the clearest identification of the end of the T wave.

A ‘U’ wave is a small deflection which occurs at the end of the T wave and may make the end of the T wave difficult to determine. U waves can occur in hypokalaemia, bradycardia, hypertrophy, central nervous system events and as a result of medication (Garcia and Holtz, 2001). If the presence of a U wave makes identification of the end of the T wave impossible in all the leads recommended for measurement, the ‘tangent’ method may be used. This method projects the end of the T wave as demonstrated in Figure 3.

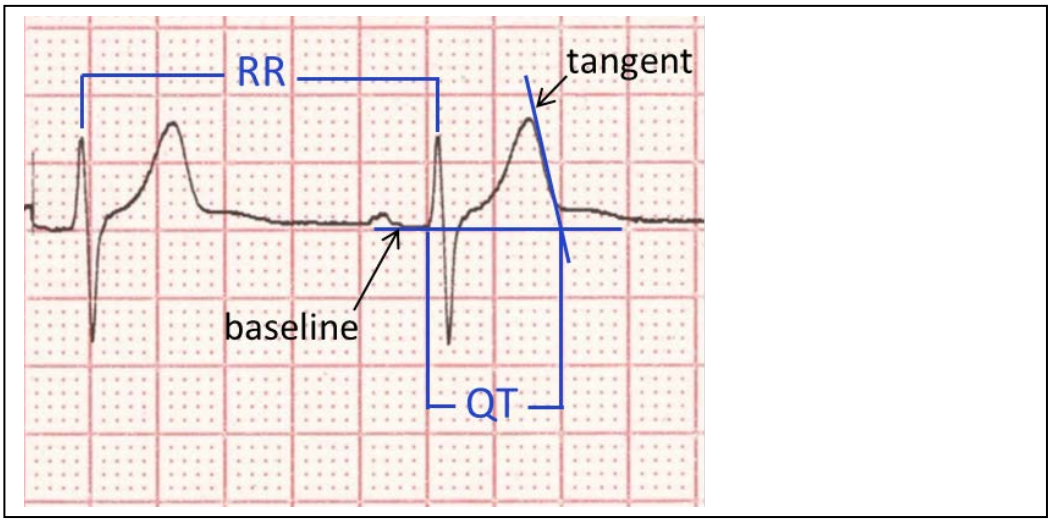

Figure 3: illustration of the 'tangent' method of identifying the end of the T wave

Postema et at (2008) found that using the tangent method resulted in inexperienced ECG readers being able to accurately and reproducibly diagnose prolonged and normal QT intervals and therefore improved stratification for LQTS.

Application of Bazett’s formula for correcting QT interval (ECG in figure 3)

1. Measure QT interval.
QT = 10 small squares. 1 small square represents 40ms, so **QT = 400ms**

2. Measure RR interval.
RR = 27 small squares. 1 small = 0.04s, so **RR = 1.08s** (RR interval *must* be expressed in seconds)

3. Find the square root of the RR interval value.
√1.08 = **1.04**

4. QTc = QT/√RR
So QTc = 400ms/1.04 = **385ms**

Nowhere in the field of QT assessment is there more variation in opinion than on the subject of what should be considered normal. Any clinician searching the literature for a value representing the upper limit of normality for QTc so that sufferers from LQTS can be reliably identified will be left puzzled and dissatisfied by the plethora of conflicting recommendations. The reason for this is simple: there is a large degree of overlap in QTc between the normal population and people with genetically proven LQTS. As a consequence there is not, and can never be, a simple cut-off value which will discriminate between those who have and those who do not have LQTS.

The QT interval also varies slightly according to sex and age; in childhood, male and female values are similar but they diverge in adolescence and in adult females the QT is approximately 10ms longer than in adult males (Rautaharju et al, 1992). In old age, male and female values are similar again. The AHA and NICE (2010) recommends that the upper limits of normality should be considered 450ms for males and 460ms for females. The clinical significance of a QTc above these limits depends on its actual value and the context in which it is found, as may be illustrated by the following example. If on routine screening, a QTc of 470ms is found in an asymptomatic male with no relevant family history, this may lead to a suspicion of LQTS. The QTc is certainly above the normal limit, yet 1 in 100 of the normal adult male population has a QTc of at least 470ms. The prevalence in the population of LQTS may be as high as 1 in 2,000, and up to 40% of genetically positive LQTS sufferers have a ‘normal’ QTc (Vincent et al, 1992). Therefore the proportion of the population who have LQTS with a QTc of at least 470ms may be 1 in 3,300. This means that an adult male with a chance finding of a QTc of 470ms is at least 33 times more likely *not* to have LQTS than to have it. However, in contrast, if the asymptomatic child of a parent with LQTS has a QTc of 440ms, even though this value is ‘normal’ there is a 50% probability that the child has LQTS (Johnson and Ackerman, 2008).

We support the AHA recommended upper limits of 450ms for males and 460ms for females but counsel caution in their application: the longer the QTc, the greater is the risk of QTc but the value must always be interpreted in the clinical context; there is no simple *cut-off that allows discrimination between normality and disease.* As a general rule, the longer the QTc, the higher is the risk of sudden death, and patients with a QT duration of greater than 500ms are at the highest risk of becoming symptomatic by the age of 40 (Priori et al, 2003, cited in ESC, 2006).

Rather than confirm or exclude the diagnosis of LQTS on the basis of a single QT measurement, a points scoring system devised by Schwartz in 1985 (Schwartz, 1985), and subsequently revised eight years later (Schwartz et al, 1993), aimed to integrate clinical history, family history, QT measurement and other relevant information by ascribing points to the presence of various criteria which when totaled would indicate the probability of LQTS. Although it has high specificity, the Schwartz system has been described as too lacking in sensitivity for clinical use (Hofman et al, 2007). Exercise testing may be helpful in risk stratifying patients for LQTS (ACC/AHA/ESC, 2006); in LQTS the QT may lengthen rather than shorten as the heart rate increases upon exercise.

Manual measurement of QT

In order to manually calculate the QT and correct it for rate the following check list may be helpful.

1. Perform a good quality 12 lead ECG using the Society of Cardiological Science and Technology guidelines (SCST, 2010).
2. Check leads II, I, III and V5 for a defined QT to measure
3. If there is a defined end to the T wave, use Bazett's formula to calculate the QTc (QTc = QT ÷ √R-R)
4. If there is no defined end to the T wave, use the tangent method, and then apply Bazett's formula.

5. Is the rhythm regular? If not, choose the longest and shortest R-R intervals and use steps above to calculate the QTc's, then average the result.
6. Once a QTc has been calculated consider:
    a. Is the QTc greater than 500ms? If yes this is almost certainly LQTS and requires urgent referral to a cardiologist specializing in cardiac rhythm management
    b. Is the QTc > 450ms for males and 460ms for females? If so, risk stratification for LQTS is required (consider Schwartz criteria) and referral to a specialist.
    c. Is the QTc <350ms? If so, consider short QT syndrome and review by specialist.
    d. Patient age: women may have a longer QT post-adolescence.
    e. Patient history: if the patient has experienced loss of consciousness or family history of sudden cardiac death (below the age of 40) this is a 'red flag' requiring urgent referral to a specialist (NICE, 2010) even if the QTc is deemed normal.

Computer measurement of QT

In view of the difficulties in measuring the QT manually it may be tempting to rely on the automatic measurement and calculation of QTc that is provide by the interpretative software in many ECG machines. However, the designers of the software face the decisions that that are so problematic for anyone manually measuring and assessing the QT. Which lead(s) should be used? How should the end of the T wave be defined? How should the QT be corrected for the heart rate? Unless it is known how these questions have been addressed by the interpretative software, the QT and QTc provided should not be relied on. Indeed, it is known that different automatic measuring techniques will produce different QT intervals from the same ECG (McLaughlin et al, 1995). Moreover, even if the QT and QTc are measured and calculated accurately and in accordance with accepted guidelines, the QTc may not be correctly classified by the software as normal or prolonged

(Miller et al, 2001). We therefore recommend that the QT interval always be measured manually.

What to do if you suspect a LQTS

To confirm the diagnosis and begin the process of treating the person with the suspected LQTS and their family, a multi disciplinary approach will often be adopted although there may be regional variations. In order to meet the Department of Health (2005) aim that patients should receive 'timely assessment by an appropriate clinician to ensure accurate diagnosis and effective treatment and rehabilitation', the patient should be referred to a Cardiac Rhythm Management team. This will provide expert review of the 12 lead ECG, risk stratification and further investigations if required. For acquired or drug induced LQTS consideration should be given to external factors altering the QTc. There are support sites such as www.qtdrugs.org to help identify the medication responsible.

The multi-disciplinary team will include a cardiologist specializing in electrophysiology, specialist nurses, physiologists and may involve geneticists. In inherited cardiac conditions screening may be required to determine if other family members may be at risk and genetic testing may be part of this process. Patient support groups such as the Arrhythmia Alliance, Cardiac Risk in the Young (CRY) and British Heart Foundation provide excellent material to help the patient and their family make sense of this worrying and complex diagnosis.

Key Points

- QT measurement is complex
- The tangent method may be helpful in identifying the end of the T wave.
- QTc calculation using Bazett's formula may be inaccurate but it is still the preferred method.

- There is no single cut-off value for QTc that allows reliable discrimination between LQTS and normality. If a patient presents with a long or borderline QT that you are concerned about you should refer to the local Cardiac Rhythm Management Consultant or team.
- In the event of a sudden unexplained death think 'genetics', review the family history and gain a specialist opinion. Screening of first-degree relatives may prevent another death.

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