Short QT
When Does It Matter?

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For half a century, the relationship between the QT interval and cardiac arrhythmias has been recognized, although attention has focused primarily on prolongation of the QT. The congenital long-QT syndrome (LQTS) was first identified in patients with syncope, aborted sudden death, or family history of cardiac arrest as an association between a prolonged QT interval and development of potentially fatal polymorphic ventricular tachycardia (torsade de pointes). Further research has resulted in the identification of a number of etiologic inherited ion channelopathies, and criteria have been defined to allow diagnosis and evaluation of risk based on the QT interval. Only in recent years has attention been paid to short QT intervals with the recent discovery of a familial syndrome characterized by short QT interval and sudden death (the short QT syndrome [SQTS]). In this issue of Circulation, Anttonen et al add to our understanding of the frequency of a short QT interval and prognosis in a general population.

A connection between short QT and sudden cardiac arrest was identified as early as 1993 with an association of increased mortality in patients with both QTc≥440 ms and QTc<400 ms. Since that time, the SQTS has been defined, and 4 ion channel mutations have been associated with a rapid repolarization phase of the cardiac action potential, abbreviated QT interval on 12-lead ECG, and predilection to sudden cardiac death. 

It may be that formerly “idiopathic” ventricular fibrillation relates to a shortened QT. In 1 study, 35% of men with idiopathic ventricular fibrillation were noted to have short QTc intervals (defined as QTc <360 ms) versus only 10% of men in a similar group of healthy subjects. Although studies confirm an association of sudden death with short QT, the clinical utility of such information remains unclear. Although SQTS is rarely diagnosed, ECGs are recorded frequently for any number of reasons, and as with any test there is variability in the results obtained. In the clinical setting, we must ask the question, “How short is too short, and what to do when we identify a short QT?” Data that allow us to address this question are scant. Algra et al reported in 1993 an increased risk with shorter QTc, with 400 ms as the cut-off, such that 22% of 6693 subjects were included. In contrast, a recent study of >12 000 ECGs, recorded for occupational health reasons, defined short QTc as the lowest 0.5%; the shortest QTc observed was 335 ms, and over nearly 8 years there were no deaths in the group with the shortest QTc (although follow-up was available on only 35 of the 65 patients in this cohort).

Anttonen and colleagues explore the prevalence of short QT in the general population. They report a retrospective analysis of ECGs from 10 822 randomly selected middle-aged men and women with a mean age of 44 years in which they used the Bazett’s, Fridericia, and nomogram methods to compute the QTc. They found, at most (depending on method of correction), a frequency of 0.1% for QTc <320 ms, and 0.4% for QTc <340 ms. There was no difference in the all-cause or cardiovascular mortality between subjects with a very short QTc (<320 ms) or short QTc (<340 ms) and those subjects with a normal QT interval (QTc 360 to 450 ms). In fact, cardiovascular mortality was lower for subjects with a short QT interval (adjusted hazard ratio, 0.71; 95% CI, 0.43 to 1.15) compared with those with a QTc of 360 to 449 ms. However, the event rate was extremely low with only 5 cardiovascular deaths (and no sudden deaths) among those with a QTc <340 ms. These data seemingly contradict the findings of Algra et al who noted an increased relative risk of sudden death in their short QT subgroup; however, the definitions of short QT varied in these 2 studies. Even taking into account the rare occurrence of a short QT, clinicians should be aware of the range of normal values of the QT interval and how to calculate the QTc. The consequences of missing this finding can be devastating for some individuals.

The authors are to be commended for strict attention to the methodology of QT measurement and correction for heart rate because measurement of the QT interval is not trivial. The result of this relatively low-tech procedure may have substantial impact on the quality of life and survival for at-risk individuals such as those patients considered for possible LQTS. However, even cardiologists have been shown to perform poorly on measurement of QTc and identification of the ECG of patients with LQTS. In a specialty clinic for LQTS evaluation at the Mayo Clinic, 73 of 176 (41%) patients with previous diagnosis were found not to have LQTS largely on the basis of modified interpretation of the ECG; in some cases these patients had already undergone implantable cardioverter defibrillator implantation.

Moss and colleagues recently provided a valuable methodological paper on measurement of the QT interval. A 12-lead
ECG tracing at a paper speed of 25 mm/s at 10 mm/mV is usually adequate to make accurate measurements of the QT interval. The QT is assessed as a mean value of at least 3 to 5 cardiac cycles measured as the time duration in milliseconds from the beginning of the earliest onset of the QRS complex to the end of the T wave, using leads II and V5 or V6 and choosing the longest identified. The end of the T wave is the point at which the descending limb of the T wave intersects the isoelectric line (as was performed by Anttonen et al). Much of the uncertainty exists within this determination of the end of the T wave, especially when there are overlapping T and U waves. With the presence of U waves, it becomes difficult to identify the exact intersection of the T wave with the isoelectric line; in these situations, the authors advocate measurement of both the QT interval and the QTU interval (taken to the end of the U wave as it intersects the isoelectric line) because the QTU interval reflects the total duration of ventricular depolarization.

Heart rate correction is required for adequate assessment of the QT interval. Various correction formulas have been developed, the most common being Bazett’s: QTc is equal to QT interval in seconds divided by the square root of the R-R cycle length in seconds. Bazett’s correction performs less well at high and low heart rates, whereas the cube root Fridericia formula performs better with low heart rates. The nomogram method, used in the present study along with the Bazett and Fridericia methods, may have advantages across the full range of heart rates (40 to 120 beats per minute), but is rarely employed. Manual measurements and calculation of the corrected QT intervals become essential for assessment of the QT intervals on 12-lead ECGs because computer analysis is often erroneous.

In general, a QTc (by Bazett’s correction) is considered prolonged at >450 ms for adult men and >470 ms for adult women. As opposed to a prolonged QT interval, there is no uniformly accepted value for the lower limit of the QTc. However, Viskin et al used a value of QTc <360 ms in men and QTc <370 ms in women for a designation of short QT based on the fact that this value represents the lowest 0.5% of the distribution of QTc intervals in the normal population. Rautaharju et al investigated the variation in QT interval in a population of 14,379 healthy individuals and suggested that values of QT below and above 2 SD from the mean should be considered either short or long QT values. They defined a prevalence of 0.4% (360 individuals) for either a prolonged or short QT on the basis of the 2-SD cutoff from the mean (mean QT = 374 ms, short QT ≤319 ms, prolonged QT ≥430 ms), a similar occurrence to that found in the present study. The authors of the present study used values of 320 ms and 340 ms and noted that there are no reported cases of SQTS with a QTc >340 ms.

The present study contributes significantly to the literature regarding SQTS. The authors took great care to measure the QT and adjust for heart rate with relevant methodology. The patient population was large (n=10,822) and follow-up was both long (29±10 years) and remarkably complete in Finland’s Social Insurance Institution’s Coronary Heart Disease Study. Limitations persist, however. This is a retrospective study of ECGs obtained on the participating subjects; therefore, conclusions based on these data need to be put into the correct context. Furthermore, generalization of the results is limited because only middle-aged subjects were included (ages 30 to 59 years); reports of familial SQTS include a number of individuals <30 years old, so perhaps some younger patients with short QT did not survive to allow enrollment in the study. Generalization to a more ethnically heterogeneous population may also be difficult because this study included a homogeneous Finnish population from 1966 to 1972. Finally, the small number of subjects with a short QT interval in this population renders the study underpowered to assign prognostic value to an incidental ECG finding of a short QT. For example, there were only 11 subjects with QTc <320 ms, and no sudden death events were reported. This provides little reassurance because the 95% confidence intervals around an incidence of 0 out of 11 would include frequencies that might even allow for prophylactic implantable cardioverter defibrillator implantation.

How should we put the findings of the study by Anttonen et al into the context of patient care? The present report and earlier literature suggest that a short QT interval on 12-lead ECG does not by itself predict risk of life-threatening arrhythmias but rather should be taken in context of each individual patient. On the other hand, because the present finding is rare, one should consider SQTS in a patient with QT <340 ms and other factors suggestive of arrhythmia (such as syncope or family history of sudden death). As further genetic etiologies for SQTS are identified (with their prevalence evaluated in asymptomatic populations with shorter QT intervals), and testing becomes more uniformly accessible, we can look to a day when we will be able to either easily identify the presence of a high-risk mutation or reassure the patient that the risk is indeed low.

Disclosures

Dr Viswanathan has no disclosures. Dr Page is a consultant to sanofi-aventis and has been a consultant to Berlex Laboratories and Reliant Pharmaceuticals. He has been a consultant to and received grant support from Procter & Gamble Pharmaceuticals.

References


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