Abnormal QT responses to adenosine in subjects with long-QT syndrome

In the interesting article by Viskin et al., adenosine-induced bradycardia was found to produce a higher increase in QT and a lower decrease in QTc (calculated using the Bazett formula) in subjects with long-QT syndrome (LQTS) than in controls. However, a major issue in this study concerns the reliability of QT correction when large ranges of heart rates are analysed. The Bazett formula overcorrects at slow rates and undercorrects at high rates.2 More generally, the accuracy of correction formulas is limited by the high inter-individual variability of the QT/RR relation, so that they should only be used for an approximate adjustment of QT over a narrow range of heart rates.4 In the study by Viskin et al., mean RR interval ranged from 580 to 1670 ms in the LQTS group, and from 550 to 2240 ms in the controls. These wide ranges suggest that caution is required in interpreting the observed between-group differences in QTc.

Moreover, the appropriateness of QT correction during abrupt changes in heart rate should be considered critically. Most correction formulas utilize models obtained by rest electrocardiograms in subject cohorts, but do not describe the electrophysiological process of delayed adaptation of repolarization to rapid changes in heart rate, i.e. QT hysteresis. Although QT correction has been used in studies on LQTS patients under dynamic conditions such as epinephrine administration, measurements were generally taken at steady state during infusion.3 The effect of QT hysteresis throughout the sudden adenosine-induced deceleration-acceleration sequence may be reasonably relevant. Therefore, when QT is adjusted to the preceding RR interval in these conditions, the resulting value does not represent an effectively rate-corrected QT (i.e. it does not reflect the QT expected at 60 bpm). Also, this value has controversial biological meaning, because it is derived by applying formulas calculated in steady-state conditions to data recorded in non-steady-state conditions.

An alternative analysis could be performed using the QT/RR plot obtained over a few minutes of recording during the test. This may allow (i) avoidance of bias due to QT correction over large RR ranges; (ii) quantification of QT hysteresis by evaluation of the QT/RR loop; and (iii) estimation of QT/RR slope, obtained either from raw data or after QT lag compensation by resynchronization of QT and RR changes.6 This analysis might also be helpful in differentiating among different LQTS genotypes. QT hysteresis could differ between genotypes, as shown by different dynamic responses to sympathetic stimulation.7 Also, the higher increase in QT at maximal bradycardia in the LQTS group than in healthy subjects shows steeper QT/RR slope in LQTS patients than in healthy subjects.8 However, current evidence suggests that an increased QT/RR slope exists in LQTS and particularly in LQT3 patients, but not in those with LQT1 genotype, as in these subjects, a paradoxical prolongation in QT occurs at fast rates.9,10 On the basis of these considerations, dynamic assessment of QT rate dependence and hysteresis could be clinically intriguing and may improve the diagnostic accuracy of the adenosine challenge test.

References


Abnormal QT responses to adenosine in subjects with long QT syndrome: reply

We agree with Dr Ballo that understanding the significance of specific QTc values observed during the sudden heart rate slowing and acceleration provoked by adenosine, in patients with long-QT syndrome (LQTS), is problematic. Clearly, the QTc values obtained during the extreme bradycardia or tachycardia provoked by adenosine should not be defined as ‘normal’ or ‘prolonged’ on the basis of the time-honoured literature on the LQTS, which relates to values during undisturbed heart rate at rest. Instead, the QTc values during the adenosine test should be viewed in comparison with those of a large control population undergoing the same test. Moreover, the following observations suggest that the observations presented in our study on the use of the adenosine challenge test for diagnosing LQTS1 are valid. (i) The heart rate deceleration provoked by adenosine was similar in patients and controls. If anything, controls developed slower heart rate during the bradycardia phase of adenosine (RR interval of 2240 ± 1270 ms in controls vs. only 1670 ± 670 ms in LQTS, \( P = 0.09 \)). However, the absolute (i.e. uncorrected) QT interval increased much more in LQTS patients. In fact, the absolute QT of controls hardly changed despite the marked and sudden bradycardia (the QT of controls increased by only 1.5 ± 6.7% in comparison with their baseline). In contrast, the uncorrected QT of patients with LQTS increased during similar degrees of bradycardia by 15.8 ± 13.1% (\( P < 0.001 \)). (ii) Similar arguments can be made about the tachycardia-induced QT changes provoked by adenosine. Despite similar degrees of adenosine-induced heart rate acceleration, not only the QTc, but also the absolute (uncorrected) QT intervals were much longer in LQTS patients (Figure 1 in our article).1 In addition, except for T-wave inversion (which was a non-specific finding), bradycardia and/or tachycardia-induced changes in T-wave morphology were of diagnostic value (Figures 3 and 4 in our article).1 As described for the epinephrine-challenge test,2 appearance of notched T-waves during our adenosine challenge test (especially when the second component of the T-wave was tall) was highly suggestive of LQTS.1

We agree with Dr Ballo that it is likely that patients with LQT3 will develop steeper QT prolongation during the bradycardia phase of the adenosine test, whereas LQT1 patients will develop QT changes only during the tachycardia phase. However, we do not have sufficiently large number of genotyped patients and we hope that other groups will eventually test this hypothesis.

References

Corrigendum to: ‘Effects of nebivolol in elderly heart failure patients with or without systolic left ventricular dysfunction: results of the SENIORS echocardiographic substudy’ [Eur Heart J 2006;27:562–568]

Stefano Ghio, Giulia Magrini, Alessandra Serio, Catherine Klersy, Alessandro Fucili, Aleksandr Ronaszkevičiūnas, Pal Karpati, Giacomo Mordenti, Angela Capriati, Philip A. Poole-Wilson, and Luigi Tavazzi on behalf of the SENIORS investigators

Regrettably, the spelling of the author’s name Alessandro Fucili was published as ‘Alessandro Fucilli’ with two l’s in the surname. This was incorrect and should have appeared as ‘Fucili’. The author apologizes for this error.