LQT2 variant

Dr. Andrés R. Pérez Riera

LQT2 variant is due to a chromosomal mutation affecting the HERG gene (human ether-a-go-go gene) that encodes the rectifying rapid outward potassium Ikr channel in phase 3 of cardiac action potential.

In this variant, the arrhythmic events are triggered by noises (clock alarms), emotions or stress.

ECG is characterized by QT interval prolongation with bifid T wave and of low amplitude (T1-T2), with T1-T2 interval <150 ms.

When measuring the QT interval, the ECG is best recorded at a paper speed of 50 mm/s and at an amplitude of 0.5 mV/cm using a multichannel recorder capable of simultaneously recording all 12 leads. A tangent line to the steepest part of the descending portion of the T wave is then drawn. The intercept between the tangent line and the isoelectric line is defined as the end of the T wave.

The QT interval is measured from the beginning of the QRS complex to the end of the T wave on a standard ECG. There are no available data on which lead or leads to use for QT interval measurement. Traditionally, lead II has been used for QT interval measurement because in this lead, the vectors of repolarization usually result in a long single wave rather than discrete T and U waves. Generally, QT prolongation is considered when the QTc interval is greater than 440 ms (men) and 460 ms (women), although arrhythmias are most often associated with values of 500 ms or more. The severity of pro-arrhythmia at a given QT interval varies from drug to drug and from patient to patient.

Unfortunately, the extent of QT prolongation and risk of TdP with a given drug may not be linearly related to the dose or plasma concentration of the drug because patient and metabolic factors are also important (for example, sex, electrolyte concentrations, etc). Furthermore, there is not a simple relation between the degree of drug induced QT prolongation and the likelihood of the development of TdP, which can occasionally occur without any substantial prolongation of the QT interval.

The QT interval is influenced by heart rate. The RR interval preceding the QT interval should be measured for rate correction. Several formulae may be used to correct the QT interval for the biophysical effect of heart rate (QTc), but none is perfect. The most commonly used formulae are Fridericia's cube root formula (QTc = QT/RR1/3) and Bazett's square root formula (QTc = QT/RR1/2). Of the two, Bazett's formula is the more popular, but Fridericia's correction is preferred because it is more accurate at the extremes of physiological heart rate.

Apart from heart rate, the duration of the QT interval is also subject to the techniques of recording and measurement error of the QT interval, sympathovagal activity, drugs, genetic abnormalities, electrolyte disorders, cardiac or metabolic diseases, changes of cardiac afterload, and diurnal variation which can be up to 75–100 ms. The authors from the Masonic Medical Research Laboratory in Utica, NY, USA, suggest that the "M" cells present in the mid myocardium have a repolarization time more prolonged than the endo and epicardial cells (comparable to Purkinje cells), and they could be responsible for congenital or acquired long QT syndrome. In long QT syndromes, a U wave would be caused by M cells in the mid myocardium
The electrophysiological features of M cells are summarized as follows:

1) Phase 0 wider than in the endocardial and epicardial cells (greater dromotropism), and minimally less wide than Purkinje cells;
2) Phase 1 with marked notch similar to epicardial cells and different from endocardial cells that do not present notch. This significant notch indicates a strong initial Ito outward potassium channel;
3) Phase 2 long and in plateau similar to Purkinje cells.