CORRELATION OF MUTATION LOCATION AND ION CHANNEL CHARACTERISTICS WITH CARDIAC EVENT TRIGGERS IN LONG QT SYNDROME TYPE 1

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Background: Risk factors for cardiac event triggers have not been previously investigated in the long QT syndrome type 1 (LQT1) population. The aim of this study was to evaluate the association between clinical and genetic factors and functional channel properties and the triggering factor for cardiac events in LQT1 patients.

Methods: Cox proportional hazards regression modeling was utilized to assess the risk of a first LQTS-related cardiac event (syncope, aborted cardiac arrest or death) according to type of trigger among 574 genetically-confirmed LQT1 patients from the US portion of the International LQTS Registry.

Results: One hundred and ninety three patients experienced cardiac events, of whom 121 events (63%) were associated with exercise triggers, 31 events (16%) were associated with arousal triggers, and 41 events (21%) were associated with non-exercise/non-arousal triggers. Male gender (HR=1.88; p=0.004), QTc >500 msec (HR=3.01; p<0.001), mutation location in the cytoplasmic loops (HR=5.09; p<0.001 [Figure]), and tau of activation >1.21 (HR=3.37; p=0.001) were associated with exercise-triggered events, whereas only cytoplasmic loop location (HR=7.66; p=0.007) was independently associated with arousal-triggered events.

Conclusion: Clinical and genetic risk factors can be used to identify LQT1 patients with increased risk for exercise and arousal-triggered cardiac events.

Figure: Kaplan Meier estimate of the cumulative probability of exercise triggered first cardiac event in LQT1 patients by mutation location