Utility of Automated QT Analysis on Holter Monitors in the Diagnosis of Long QT Syndrome

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Background: Long QT syndrome (LQTS) is a potentially lethal channelopathy affecting 1 in 2,500 people. Referral to cardiology for evaluation of prolonged QTc is common and increasing with disease awareness, inaccurate QTc calculation, and misinterpretation of normal QTc distribution. However, diagnosis can be challenging due to significant overlap of normal and abnormal QTc ranges. Ambulatory electrocardiographic monitoring (Holter) has had limited diagnostic value due to infrequent arrhythmia and limited correlation of absolute QT interval values compared to 12-lead ECG. We hypothesized that automated QT analysis on Holter monitors would demonstrate a significant difference between LQTS and control patients.

Methods: We conducted a retrospective review from January 2010 to January 2016 of patients with known genotype positive, phenotype positive LQTS who underwent Holter testing. Age and gender matched control patients were selected at a ratio of 2:1. Automated QT analysis data was collected including minimum, mean, and maximum values for QT and QTc intervals, as well as percent QTc intervals >450 ms. Data was compared using conditional logistic regression and receiver operator curves were generated.

Results: Thirty-nine genotype positive, phenotype positive LQTS patients and 78 matched controls were identified. There was no difference between cohorts in age, gender, or race. Significant differences were found in all automated QT and QTc fields, except minimum QTc interval (p=0.57). Mean QTc interval (LQTS 479 ± 28 ms vs controls 429 ± 16 ms; p=<0.001) and percent QTc intervals >450 ms (LQTS 80 ± 28% vs. controls 14 ± 16%; p=<0.001) were selected for further analysis and a ROC was generated for each variable. Both curves demonstrated high area under the curve values of 0.9494 for average QTc and 0.9540 for percent QTc intervals >450 ms. Threshold values of ≥461 ms for mean QTc (sensitivity 79.49%, specificity 98.72%) and ≥65% of QTc intervals >450 ms (sensitivity 79.49%, specificity 98.72%) allowed highly specific discrimination between LQTS and healthy controls (false positive rate 1.09%). Similarly, thresholds of <434 ms (sensitivity 97.44, specificity 61.54) for mean QTc and <32% (sensitivity 89.74, specificity 87.18) for percent QTc >450 ms resulted in highly sensitive discrimination (false negative rates 4.35% and 8.7% respectively).

Conclusion: Holter monitor testing with automated QT analysis appears to be a highly sensitive and specific method for differentiating between patients with LQTS and healthy controls. Threshold values for mean QTc interval and percent of QTc intervals >450 ms could potentially be utilized in concert with existing diagnostic algorithms as a screening tool for LQTS.