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UTILITY OF TREADMILL TESTING AND DCG IN DIAGNOSIS OF LONG QT SYNDROME

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Background The hereditary long QT syndrome (LQTS) is a genetic channelopathy that is characterised by a prolonged QT interval, syncope, ventricular arrhythmias, and sudden death. The clinical diagnosis of LQTS remains challenging when ECG abnormalities are borderline or intermittent. And although genetic testing remains the diagnostic gold standard, it is not readily available. Evaluation of the rate adaptation of QT intervals may help in establishing the diagnosis of LQTS.

Objective To investigate whether treadmill test and dynamic electrocardiogram (DCG) could help to identify LQTS patients and distinguish LQT1 from LQT2 genotypes.

Methods Treadmill test group: a modified Bruce protocol treadmill exercise test was performed in 45 healthy subjects and 18 patients with LQTS (15 LQT2, 3 LQT1), with ECGs recorded at the end of every Bruce protocol level during exercise, at peak exercise, and at 2 min intervals during the recovery phase. The QT intervals, QTa intervals, T peak to T end intervals (Tp-Te intervals) and QT dispersion were measured at these ECGs. Rate adaptation of QT was studied as QT/heart rate slopes. Dynamic electrocardiogram group: DCGs were performed in 26 healthy subjects and 27 patients with LQTS (19 LQT2, 7 LQT1, 1LQT3). The QT intervals and Tp-Te intervals were measured at the maximal, minimal and mean heart rate.

Result Treadmill test group: (A) LQTS patients had significantly longer QT intervals and corrected QT (QTc) than healthy subjects through exercise and recovery period ($p < 0.05$). At the end of recovery, a QTc cut-off value of 470 ms distinguished 83.3% of LQTS patients from unaffected controls, and the specificity can reach 93.3%. During recovery, QTc intervals lengthened excessively in LQTS patients in comparison with controls (43.38 ± 55.11 ms, 17.11 ± 43.63 ms, $p = 0.05$). (B) The QT/heart rate slopes were significantly steeper in LQTS patients (-2.208 to -3.544) than in controls (-1.504 to -1.560) during exercise and recovery. (C) LQTS patients had longer QTa intervals at early exercise and recovery period. LQT1 patients prolonged QTa intervals as heart rate increased, whereas LQT2 patients shortened QTa intervals. (D) LQTS patients had longer Tp-Te intervals at Bruce level three and four, peak exercise and 2, 6 min into recovery period. LQT2 patients had longer Tp-Te intervals than LQT1. (E) LQTS patients had significantly longer QTd than healthy subjects through exercise and recovery period. (F) The QT/heart rate slopes were steeper in LQT2 patients than in LQT1 patients during exercise, and the two group showed a distinct pattern of QT adaptation during recovery. The progressively decreasing QT pattern as heart rate decreased was present in LQT1 patients, while the rising QT pattern was seen in LQT2 patients. Dynamic electrocardiogram group: (A) LQTS patients had significantly longer QT intervals and corrected QT (QTc) than healthy subjects at each heart rate. At the minimal heart rates, QT intervals lengthened excessively in LQTS patients (84.93 ± 56.09 ms) in comparison with controls (32.60 ± 26.51 ms, $p = 0.000$). (B) LQTS patients and controls both have the longest QTa intervals at minimal heart rates, and LQTS patients had longer QTa intervals than controls at mean and minimal heart rates. As heart rates increased, QTa intervals shortened insufficient in LQT1 in comparison with LQT2. (C) LQTS patients and controls both have the longest Tp-Te intervals at minimal heart rates, and LQTS patients had longer Tp-Te intervals than controls at maximal and minimal heart rates. LQT2 had longer Tp-Te intervals than LQT1. (D) LQT1 patients demonstrated longest QTc intervals (551.10 ± 53.29 ms) at the maximal heart rates, whereas LQT2 patients demonstrated longest QTc intervals (530.16 ± 73.85 ms) at the mean heart rates.

Conclusion During exercise period, QT intervals shortened sufficiently in LQTS patients as with healthy subjects, which was consistent with LQT2 subtype. The QT/heart rate slopes were steeper in LQT2 patients than in LQT1 patients during exercise, which revealed the severe defect of repolarisation reverse in LQT1 patients, and the two group showed a distinct

pattern of QT adaptation during recovery. QTa, Tp-Te intervals and QTd facilitated diagnosing and genotyping LQTS.