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Abstract: AIMS: Torsades de pointes arrhythmias (TdP) occur by definition in the setting of prolonged QT intervals. Animal models of drug induced Long-QT syndrome (dLQTS) have shown higher predictive value for proarrhythmia with beat-to-beat variability of repolarization duration (BVR) when compared with QT intervals. Here, we evaluate variability of QT intervals in patients with a history of drug-induced long QT syndrome (dLQTS) and TdP in absence of a mutation in any of the major LQTS genes. METHODS AND RESULTS: Twenty patients with documented TdP under drugs with QT-prolonging potential were compared with 20 matched control individuals. An observer blinded to diagnosis manually measured lead-II, RR, and QT intervals from 30 consecutive beats. BVR was determined from Poincaré plots of QT intervals as short-term variability (STV(QT) = Sigma[QT(n)(+1) - QT(n)]/[30 x radical2]). QRS interval and cycle length was comparable between study groups and controls. No difference was found in QTc between dLQTS and controls (428 +/- 25 vs. 421 +/- 34 ms, P = 0.26), whereas STV(QT) was significantly higher in dLQTS when compared with controls (8.1 +/- 3.7 vs. 3.6 +/- 1.3 ms, P = 0.001). Proarrhythmic predictive power of STV(QT) was superior to that of the QTc interval (AUC: 0.89 vs.
CONCLUSION: In the absence of QTc prolongation, baseline STV(QT) characterized patients with documented drug-induced proarrhythmia. STV(QT) could prove to be a useful non-invasive, easily obtainable parameter aiding the identification of the patient at risk for potentially life threatening arrhythmia in the context of drugs with QT prolonging potential.