Relation of increased short-term variability of QT interval to congenital long-QT syndrome.

Abstract:
Apart from clinical symptoms the diagnosis and risk stratification in long-QT syndrome (LQTS) is usually based on the surface electrocardiogram. Studies have indicated that not only prolongation of the QT interval but also an increased short-term variability of QT interval (STV(QT)) is a marker for a decreased repolarization reserve in patients with drug-induced LQTS. The aims of this study were to determine if STV(QT) (1) is higher in patients with LQTS compared with controls, (2) if this effect is more pronounced in a high-risk LQTS population, and (3) could increase the diagnostic power of the surface electrocardiogram in identifying mutation carriers. Forty mutation carriers were compared with age- and gender-matched control subjects in the absence of beta-receptor-blocking agents. Lead II or V(5) RR and QT intervals from 30 consecutive beats were manually measured. STV(QT) was determined from Poincaré plots of QT intervals (STV(QT) = Sigma|QT_{n+1} - QT_n|/[30 x radical2]). Compared with controls, patients with LQTS had a prolonged QTc interval (449 +/- 41 vs 411 +/- 32 ms, p = 0.00049) and increased STV(QT) (6.4 +/- 3.2 vs 4.1 +/- 1.6 ms, p = 0.005). In patients with the highest risk of clinical events, defined as a QTc interval>500 ms or symptoms before beta-blocker therapy, STV(QT) was 9 +/- 4 ms. QTc interval had a sensitivity of 43% and a specificity of
97% in identifying mutation carriers (thresholds 450 ms for men and 460 ms for women). Receiver operator characteristic analysis showed that an STV(QT) of 4.9 ms was the optimal cut-off value to predict mutation carriers. When incorporating an STV(QT)>4.9 ms for those whose QTc interval was within the normal limits, sensitivity to distinguish mutation carriers increased to 83% with a specificity of 68%, so that another 15 mutation carriers could be identified. In conclusion, these are the first results in humans showing that STV(QT) is increased in congenital LQTS, this effect is increased in patients with symptoms before therapy, and, hence, STV(QT) could prove to be a useful noninvasive additive marker for diagnostic screening to bridge the gap before results of genetic testing are available.

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