QT/RR Coupling and Gender Differences

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Data from the THEW database (72 men, 55 women) was used to test various QT/RR models and gender differences. Three dynamic models (transfer function model TRF, exponential weighting EXP, and EXP with added direct coupling with RR EXPDC) and a static nonlinear model (NONLIN) were tested. Two records (30 min) were analyzed for each subject. Sets of RR and QT intervals together with the moving average of RR and QT intervals were analyzed. The tested parameters were: QTc, QT/RR slope (GainS, slope is QT gain for slow RR variability), time constant of QT adaptation, QT gain for fast RR variability (GainF) and error signal between measured and model QT (RMS). Results: A) Gender differences: Women have longer QTc $p<0.0001$, higher level of GainS and GainF and faster QT adaptation, all $p<0.05$. B) Model differences: NONLIN has significantly higher RMS and lower QTc ($p<0.001$) relative to dynamic models. NONLIN has higher intersubject parameter differences and higher dependency on the number of averaged intervals. Dynamic models: QTc differences (paired tests) are minimal (2.4 ± 4 ms). The EXP model has significantly higher RMS $p<0.01$ than the TRF or EXPDC model. Conclusion: i) Dominant QT/RR coupling is dynamic. The nonlinear static model does not assess the proper QTc even with averaging. ii) The EXP model overestimates random QT variability (RMS); its step response differs from known QT step response. The best models are TRF and EXPDC according to the mathematical test (minimal RMS) and physiological test (shape of step response). If only QTc is analyzed, the choice of dynamic model is not important. iii) The longer QTc and steeper GainS in healthy women are compensated to an extent by higher GainF and faster QT adaptation. GainF is an important parameter. The QT dynamic differences from steady state are proportional to GainS - GainF. We hypothesize that an analysis of the influence of drugs on QT dynamic properties may explain why cardiac arrhythmias and drug-induced Torsades de Pointes are more prevalent in women. Such analysis supposes the standardization of the QT model and measurement with defined significant excitation of RR.