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ALTERATION OF THE RELATIONSHIP BETWEEN VENTRICULAR REPOLARIZATION AND
HEART RATE INDUCED BY 60-DAY HEAD-DOWN BED REST**Abstract**

Permanence in microgravity induces cardiac deconditioning, possibly affecting QT/RR relationship and increasing the arrhythmic risk. Head-Down Tilt (HDT) bed rest is a ground-based analogue model, simulating the effects of microgravity on human body. Our aim was to evaluate if 60-day HDT could induce alterations in the QT/RR relationship and spatial repolarization heterogeneity. Ten healthy volunteers were tested. For each subject, 12-lead 24-hour Holter ECG was acquired 9 days before HDT (BDC), the 5th (HDT5), 21st (HDT21) and 58th (HDT58) day of HDT, the 1st (R+0) and 8th (R+7) day after HDT. Kors regression transformation was applied to obtain the orthogonal leads X, Y, Z, and the vectorcardiogram of the night period was computed. Selective beat averaging was used to obtain averages of P-QRS-T complexes preceded by the same heart rate in the range between 900-1200 ms: for each 10-ms bin, a mean template was computed and used to extract RTapex (ms), RTend (ms), Tapex (μV), Tarea (mVms), ventricular gradient magnitude (VG (mVms)) and its spatial orientation (QRS-T angle (deg)). Changes during HDT were tested ($p < .05$, Friedman, post-hoc Wilcoxon Signed Rank, Hochberg correction). To explore the QT/RR relationship, for each parameter the median values for each bin among all subjects were linearly correlated with corresponding RR, and r^2 coefficient and slope were computed. Results showed that the RTend shortened at HDT5 (-4.2[-5.8;-2.7]%) and HDT21 (-3.7[-5.2;-2.7]%) compared to BDC, and both Tapex and Tarea decreased (respectively up to -28.6[-31.6;-23]%) and -28.9[-30.8;-26.6]%) at HDT5), as well as VG (up to -22.2[-26.9;-12.3]%) at HDT21), then recovering to baseline values at HDT58. At R+0, all parameters, except the QRS-T angle, further decreased compared to BDC (RTapex -6.2[-10;-2]%; RTend -5.9[-9.7;-4.4]%; Tapex -22.9[-34.4;-19.2]%; Tarea -25.2[-39.6;-21.3]%; VG -17[-27.4;-13.6]%), without recovering at R+7 (Tapex -15.2[-21.9;-12.5]%; Tarea -19[-23.6;-14.7]%; VG -11.1[-19.2;-9.6]%). QT/RR relation (r^2) was impaired at HDT21 compared to BDC (Tapex from 0.62 to 0.16; Tarea from 0.90 to 0.54; VG from 0.83 to 0.32; QRS-T angle from 0.84 to 0.01), associated to a slope reduction. Also, a marked correlation reduction compared to BDC appeared again at R+0 (RTapex from 0.96 to 0.30; RTend from 0.97 to 0.48; Tapex 0.07; Tarea 0.14; VG 0.16; QRS-T angle 0.31), without completely recovering at R+7. Interestingly, the clinical analysis of the ECG signals revealed an increase of the number of ventricular ectopic beats at R+0. In conclusion, nightly ventricular repolarization was affected by 60-day HDT, with major changes elicited when normal gravity was reinstated, thus possibly increasing arrhythmogenic risk.