# CARDIAC REMODELING ACCOMPANIED BY INCREASED ARRHYTHMIA SUSCEPTIBILITY IN A DOG MODEL OF CHRONIC HIGH-INTENSITY ENDURANCE TRAINING

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Despite the cardiovascular benefits of regular physical exercise, chronic high-level exercise can evoke malignant arrhythmias, including ventricular fibrillation and even sudden cardiac death, especially in young top athletes. In some cases the underlying mechanisms are unclear.
The goal of this study was to assess mechanisms underlying cardiac structural-electrical changes and arrhythmia vulnerability by high-level vigorous exercise training in animal species that are electrophysiologically relevant to the human heart.
Beagle dogs were randomly assigned to matched sedentary (‘Sed’, n=12) or intensive exercise-training (‘Ex’, n=12) groups. ‘Ex’ dogs underwent a 4-month-long intensive treadmill-running protocol (5 days a week, 6 hours a day at a speed of 14-21 km/h with an inclination 5-12%). *In vivo* echocardiography and electrophysiological measurements were performed. Proarrhythmic sensitivity was tested and the autonomic alterations were examined. At study end, arrhythmia susceptibility was tested with high-frequency burst stimulation in open-chest anaesthetized dogs. This was followed by cardiac excision and cardiomyocyte isolation, formalin preservation for histology and snap-freezing in liquid nitrogen for molecular biology.
The vigorous endurance training was resulted in increased left ventricular end-diastolic diameter, increased septal wall thickness and greater left ventricular mass index (LVMi ‘Sed’ vs. ‘Ex’: 98±12 vs. 136±7 g/m2, $p<0.05$). Some degree of enhanced fibrosis was observed. Endurance training decreased heart rate both in whole animal and *in vitro* dog experiments. ECG recordings presented enhanced heart rate variability parameters, prolonged PQ (‘Sed’ vs. ‘Ex’: 98.3±2.9 vs. 116.7±3.6 ms, $p<0.05$), QRS (‘Sed’ vs. ‘Ex’: 60.5±2.4 vs 70.8±1.6 ms, $p<0.05$), QTc (‘Sed’ vs. ‘Ex’: 213.6±2.8 vs. 237.1±3.4 ms, $p<0.05$), Tp-Te (‘Sed’ vs. ‘Ex’: 27.9±2.5 vs.36.5±1.7 ms, $p<0.05$) intervals associated with significantly enhanced QT interval variability (eg. QT-STV ‘Sed’ vs. ‘Ex’: 2.5±0.2 vs. 3.6±0.4 ms, $p<0.05$), reflecting elevated level of repolarization dispersion. Ectopic activity was also enhanced in the exercised dog ventricle. Atropine treatment resulted in moderate heart rate increase in the ‘Ex’ animals. Chronic endurance exercise elevated the proarrhythmic risk and consequent ventricular fibrillation in dogs subjected to burst electrical stimulation.
We developed a new animal model that shares similarities with the human endurance-trained athlete’s heart. The model represents increased arrhythmia susceptibility, an important clinical paradigm, and explores potential underlying mechanisms, including vagal enhancement, increased repolarization dispersion and enhanced fibrotic changes. Increased arrhythmia susceptibility is supported by the enhanced arrhythmia incidence in the exercised group. Similar changes may be present in young human top athletes, however further investigations are required.

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