題名:Tumor Necrosis Factor-α Alters Calcium Handling and Increases Arrhythmogenesis of Pulmonary Vein Cardiomyocytes

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摘要:Inflammation and abnormal calcium homeostasis play important roles in atrial fibrillation. Tumor necrosis factor-alpha (TNFalpha), a proinflammatory cytokine, can induce cardiac arrhythmias. Pulmonary veins (PVs) are critical in initiating paroxysmal atrial fibrillation. This study was designed to investigate whether TNFalpha may change the calcium handling and arrhythmogenic activity of PV cardiomyocytes. We used whole-cell patch clamp and indo-1 fluorimetric ratio technique to investigate the action potentials, ionic currents and intracellular calcium in isolated rabbit single PV cardiomyocytes with and without (control) incubation with TNFalpha (25 ng/ml) for 7-10 h. The expression of sarcoplasmic reticulum ATPase in the control and TNFalpha-treated PV cardiomyocytes was evaluated by confocal micrographs and Western blot. We found that the spontaneous beating rates were similar between the control (n=45) and TNFalpha-treated (n=28) PV cardiomyocytes. Compared with the control PV cardiomyocytes, the TNFalpha-treated PV cardiomyocytes had significantly a larger amplitude of the delayed afterdepolarizations (6.0+/-1.7 vs. 2.6+/-0.8 mV, P<0.05), smaller L-type calcium currents, larger transient inward currents, larger Na(+)-Ca(2+) exchanger currents, a smaller intracellular calcium transient, smaller sarcoplasmic reticulum calcium content, larger diastolic intracellular calcium, a longer decay portion of the calcium transient (Tau), and a decreased sarcoplasmic reticulum ATPase expression. In conclusion,

TNFalpha can increase the PV arrhythmogenicity and induce an abnormal calcium homeostasis, thereby causing inflammation-related atrial fibrillation.