題名:Calmodulin kinase II inhibition prevents arrhythmic activity induced by alpha and beta adrenergic agonists in rabbit pulmonary veins.

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摘要:The autonomic nervous system and calcium regulation play important roles in the pathophysiology of atrial fibrillation. Calmodulin regulates the calcium homeostasis and may mediate the proarrhythmic effects of autonomic nervous agents. The purpose of this study was to compare the effects of beta- and alpha-adrenoceptor agonists on the pulmonary vein electrical activity and evaluate whether calmodulin kinase II inhibitors may change the effects of the adrenoceptor agonists on the pulmonary vein arrhythmogenesis. Conventional microelectrodes were used to record the action potentials in isolated rabbit pulmonary vein tissue specimens before and after the administration of isoproterenol, phenylephrine and KN-93 (a calmodulin kinase II inhibitor). In the tissue preparation, isoproterenol (0, 0.1, 3 microM) increased the beating rates (1.5+/-0.2, 1.6+/-0.2, 2.3+/-0.3 Hz, n=10, P<0.001) with the genesis of early afterdepolarizations (EADs, 0%, 40%, 50%, P<0.05) and increased the amplitude of the delayed afterdepolarizations (DADs, 0.6+/-0.3, 1.7+/-0.4, 3.9+/-1.0 mV, P<0.05). Phenylephrine (0, 1, 10 microM) also increased the beating rates (1.4+/-0.2, 1.6+/-0.2, 1.9+/-0.2 Hz, n=12, P<0.001), incidence of EADs (0%, 8%, 50%, P<0.05) and amplitude of the DADs (0.4+/-0.2, 1.2+/-0.4, 2.6+/-0.8 mV, P<0.05). KN-93 did not change the pulmonary vein beating rates or action potential duration. However, in the presence of KN-93 (1 microM), isoproterenol (3 microM) and phenylephrine (10 microM) did not induce any EADs or DADs in the pulmonary

veins. In conclusion, calmodulin kinase II inhibition may prevent adrenergic induced pulmonary vein arrhythmogenesis.