

INFLAMMATION AND OXIDATIVE STRESS CONTRIBUTE TO ATRIAL REMODELING DURING CHRONIC MITRAL REGURGITATION

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Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia in the United States. Mitral valve disease is a common antecedent to the development of atrial fibrillation. We used a canine model to study atrial remodeling after one and six months of chronic mild to moderate mitral regurgitation (MR). There was a significant increase in the inducibility of AF after both one and six months of MR. MR increased atrial dimensions and six months of MR resulted in P wave prolongation. We observed increased fibrosis and redistribution of connexin 40 in the left atrium. Atrial mast cells were increased only after one month of MR, while neutrophil infiltrates were increased only after six months of MR. There was evidence of oxidative stress in the left atrium at both one and six months MR, as indicated by increased peroxynitrite. There were biphasic changes in the amplitude of the transient outward K⁺ current (I_{to}), with I_{to} decreased after one month of MR and increased after six months of MR when compared to controls. Alterations in I_{to} were reversed after incubation with glutathione (GSH), the primary intra-myocyte reducing agent. The sustained outward K⁺ current was reduced only after one month of mitral regurgitation, and was not altered by GSH incubation. MR results in atrial dilatation, temporally discrete immune infiltrates, induction of oxidative stress, and biphasic time-dependent modulation of potassium currents. Cardiomyopathy, AF and MR all predispose to the development of AF; however, it appears that the underlying mechanisms are disease-specific. Targeted interventions, based on the predisposing disease may provide a basis for improved pharmacologic management of AF.

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