**Background:** 5HT4, a novel hormonal trigger to AF, acts upon 5HT4 receptors on human atrial myocytes which are linked to Gi proteins to increase heart rate. The role of the various 5HT4 receptor isoforms in the pathogenesis of arrhythmias is not understood. Our study was designed to assess the effects of enalapril and candesartan on atrial tissue eNOS expression in early stages of atrial remodeling in a canine model of rapid atrial pacing.

**Methods:** 16 halothane-anesthetized adult beagle dogs underwent insertion of a transvenous lead at the right atrial (RA) appendage. Twelve dogs were continuously paced at 400 bpm for 3 days in presence of candesartan (4 dogs; 2mg/kg/day), enalapril (4 dogs; 2mg/kg/day) or without drugs (4 dogs). Four dogs served as control group. RA effective refractory period (ERP) was measured baseline and after 3 days. RA tissue eNOS expression was determined by Western-blot.

**Results:** After pacing, ERP was shorter (p=0.048) in untreated paced dogs than in controls. Tissue eNOS expression in RA tissue was found in all dogs. RA tissue eNOS expression decreased significantly (p=0.05) in paced dogs associated with an electrophysiological remodeling. Both candesartan and enalapril prevented downregulation of RA eNOS expression, however enalapril attenuated more significantly the effects on ERP.

**Conclusions:** a) Pacing induced atrial remodeling is associated with an early downregulation of atrial tissue eNOS expression; b) angiotensin-converting enzyme inhibitors prevents the changes on atrial eNOS expression and the early atrial electrical remodeling.