

sICAM-1, IFN- $\gamma$ , IL-10, and TGF- $\beta$ 1 in all three groups ( $p$  all <0.05). It was found that CTLA-4Ig could decrease the serum concentration of CRP, sICAM-1 and IFN- $\gamma$  and increase IL-10 and TGF- $\beta$ 1, but IgG1 and PBS.

**Conclusions** CTLA-4Ig fusion protein could inhibit the (del) atherosclerosis progression in apoE(-/-) mice fed on cholesterol diet and its effect might be associated with blocking B7/CD28, anti-inflammation, promoting Th2 polarisation and affecting regulate T cells.

**e0187 ENHANCED EXTERNAL COUNTERPULSATION PROTECTS VASCULAR ENDOTHELIAL CELLS FROM APOPTOSIS IN HYPERCHOLESTEROLEMIC PIGS**

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**Objective** Evidences have proved that Enhanced external counterpulsation (EECP) improves endothelial dysfunction and repairs intimal damage by increasing vascular endothelial shear stress. Based on the assumption that unbalanced apoptosis of vascular endothelial cells (VECs) may have played a pivotal role in the pathogenesis of atherosclerotic lesions, we hypothesised that long-term EECP protects VECs from apoptosis in hypercholesterolemia pigs.

**Methods** 18 male domestic pigs were randomly assigned to 3 groups: one normal control group with a normal diet (Normal,  $n=6$ ) and two hypercholesterolemia groups (HC,  $n=12$ ) fed with atherosclerosis-inducing cholesterol-rich chow diet, one of which received EECP (HC, HC+EECP,  $n=6$ , respectively). Pigs in the HC+EECP group were treated with EECP for 2 h every other day for 36 h. In the end of the study, the animals were sacrificed, and the thoracic and abdominal aortas harvested. The thoracic aortas were sampled for both scanning and transmission electronic microscopy (SEM and TEM) whereas the abdominal aortas were stained in Sudan-III of fatty streak for macroscopic evaluation. Vascular endothelial cells (VECs) were isolated from the thoracic aorta by collagenase. TUNEL was used to detect the apoptotic index of VECs. The abdominal aortas were collected for histopathological studies.

**Results** Fatty streaks or plaques were hardly found in the normal group but clearly observable in the HC group. Atherosclerotic lesions were much less severe in the EECP group than in the HC group. SEM analysis revealed that aortic VECs were irregularly arrayed, markedly desquamated, and shrank into smaller size, which indicated apoptotic events resulting in remarkable damage of endothelium in HC group. In contrast, the VECs in HC+EECP group were arrayed in a relatively streamline fashion, less desquamated and shrank, and manifested comparatively mild endothelial damage. TEM examination of aortas in HC group showed desquamated VECs loosely attached to the matrix along with foam cells, which indicated intimal damage. Apoptotic VECs at early, middle, late stage and even apoptotic bodies were visible on intimal surface. But these changes were relatively mild in EECP-treated animals. The apoptotic index in the HC+EECP group was significantly lower than that of the HC group, but still higher than that of the Normal group ((177 $\pm$ 12)%, (237 $\pm$ 23)%, (127 $\pm$ 36)%, respectively,  $p<0.05$ ).

**Conclusions** EECP alleviates hypercholesterolemia-induced atherosclerotic damage to the vascular intima and endothelium, and protects VECs from apoptosis, thereby delaying the progression of early atherosclerotic lesions. The therapeutic benefit of EECP in terms of endothelial protection may be attributed to the inhibition of VEC apoptosis.

**e0188 ENALAPRIL, IRBESARTAN AND ANG-(1-7) PREVENT ATRIAL TACHYCARDIA-INDUCED SODIUM CHANNEL REMODELLING**

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**Purpose** Recent studies indicated that the activation of renin-angiotensin system (RAS) played an important role in the development and recurrence of atrial fibrillation (AF). Angiotensin II (Ang II) plays a central role in the process of atrial electrical remodelling (AER). Some studies on interfering with RAS have demonstrated positive effects to prevent episodes of AF both in animals and in humans. Angiotensin-(1-7) (Ang-(1-7)) is a bioactive component of RAS which can counterbalance most of effects of Ang II. In the present study, the effects of ACEI enalapril, ARB irbesartan and Ang-(1-7) on  $I_{Na}$  current ( $I_{Na}$ ) densities and  $Na^+$  channel (Nav1.5) mRNA expression were examined in a canine chronic model of AF induced by rapid atrial pacing.

**Methods** For this study, 30 mongrel dogs of either sex weighing between 11 and 15 kg were randomly assigned to sham, paced, paced+enalapril, paced+irbesartan and paced+Ang-(1-7) group, six dogs in each. Rapid atrial pacing at 500 bpm was maintained for 2 weeks, while the dogs in sham group underwent pacemaker implantation, but the pacemakers were not activated to provide atrial pacing. During the pacing, the dogs in enalapril, irbesartan or Ang-(1-7) group received enalapril (2 mg/Kg/d), irbesartan (60 mg/Kg/d) or Ang-(1-7) (6  $\mu$ g/Kg/h), respectively. The whole-cell patch-clamp technique was used to record  $I_{Na}$  and RT-PCR was applied to assess possible underlying changes in cardiac  $Na^+$  channels.

**Results**  $I_{Na}$  densities were reduced by 46.96% in paced group (-32.65 $\pm$ 10.92 pA/pF) compared with sham group (-61.56 $\pm$ 14.17 pA/pF,  $p<0.05$ ). The half-activation voltage ( $V_{1/2act}$ ) and half-inactivation voltage ( $V_{1/2inact}$ ) of  $I_{Na}$  were not altered in paced group ( $p>0.05$  vs sham). Enalapril (-44.11 $\pm$ 16.76 pA/pF), irbesartan (-65.24 $\pm$ 14.79 pA/pF) and Ang-(1-7) (-66.56  $\pm$ 18.08 pA/pF) increased  $I_{Na}$  by 35.10%, 99.82% and 103.86% ( $p<0.05$  vs paced group), respectively. Enalapril, irbesartan and Ang-(1-7) hyperpolarized  $V_{1/2act}$  compared with sham and paced group ( $p<0.05$ ). The difference of  $V_{1/2inact}$  among five groups had no statistical significance. Compared with sham group, Nav1.5  $\alpha$  subunit mRNA abundance decreased dramatically in paced group ( $p<0.05$ ). Enalapril and irbesartan prevented the decrease of Nav1.5  $\alpha$  subunit mRNA expression compared with paced group ( $p<0.05$ ). Ang-(1-7) had no effects on the decrease of Nav1.5  $\alpha$  subunit mRNA expression ( $p>0.05$  vs paced group).

**Conclusion** Enalapril, irbesartan and Ang-(1-7) increase  $I_{Na}$  densities and contribute to improving intra-atrial conduction and decreasing the likelihood AF maintains. Hence, counterbalance the Ang II actions may represent an important tool to prevent atrial ionic remodelling, and perhaps a novel therapeutic approach to the prevention of AF.

**e0189 IN VIVO SPATIOTEMPORAL VISUALISATION AND QUANTIFICATION OF MESENCHYMAL STEM CELLS WITH ROSUVASTATIN IN HINDLIMB ISCHAEMIA MICE BY 3-DIMENSIONAL MOLECULAR IMAGING**

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**Background** Stem cell therapy has generated much interest in improving the function of ischaemic myocardium and peripheral