

(S, n=30). The MI model was set up in SD rats by permanent ligation of the left anterior descending coronary artery. In S group suture was through the left anterior descending coronary artery without ligation. Before and after MI, in NL group/S group and T group normal saline and Trimetazidine (0.3 mg/kg) were separately given by gavage. The changes of serum cTnI were observed at 8, 24, 48 h after MI. The changes of serum cTnI in S group was only observed at 24th hour after operations. In 1 week, 2 weeks and 4 weeks after treatment, the areas of myocardial infarction were analysed, and isovolumic systolic left ventricular maximum rate of pressure rise (+dp/dt_{max}) and isovolumic diastolic left ventricular maximum rate of pressure drop (-dp/dt_{min}) were measured to evaluate the myocardial protection effects of STV-1Na. The groups were compared with one-way analysis of variance (ANOVA) test. A value of p<0.05 between NL group and T group. But the serum cTnI level at 24 h after MI decreased in T group (22.7±5.3 ng/ml, p<0.05) compared with NL group (42.3±5.4 ng/ml). The serum cTnI level at 24 h in NL group and T group was significantly increased compared with S group (1.59±1.42 ng/ml) (p<0.01). Trimetazidine (0.248±0.021, p<0.01) decreased significantly the myocardial infarction area compared with NL group (0.362±0.027). The infarction areas in NL group (0.362±0.027) and T group (0.248±0.021) increased significantly compared with S group (0.072±0.1445) (p<0.01). In 1 week after MI, the +dp/dt_{max} in T group (7535±265) was not significantly different (p>0.05) compared with NL group (6702±329), and the -dp/dt_{min} in T group (-5511±400) was no significant difference (p>0.05) compared with NL group (-5400±339). In 2 weeks after MI, the +dp/dt_{max} in T group (8101±313) increased significantly compared with NL group (5868±412) (p<0.01), and the -dp/dt_{min} in T group (-6514±493) decreased significantly compared with NL group (-4750±463) (p<0.05). In 4 weeks after MI, in T group (7629±374) the +dp/dt_{max} increased significantly compared with NL group (5876±200) (p<0.01), and the -dp/dt_{min} in T group (-5883±436) decreased significantly compared with NL group (-4546±279) (p<0.05). The -dp/dt_{max} in T group and NL group were significantly decreased (p<0.05) compared with S group in 1 week, 2 weeks and 4 weeks after the operation. The +dp/dt_{min} in T group and NL group were increased (p<0.05) compared to S group in 1 week, 2 weeks and 4 weeks after the operation.

Conclusions Trimetazidine has myocardial protection effects on myocardial infarction and improves myocardial systolic and diastolic function in SD rats with acute myocardial infarction.

e0185 THE EFFECT OF CLASSIC MAPK/ERK5 PATHWAY ON HYPERTHERMIA INDUCED VENTRICULAR CARDIOMYOCYTES DAMAGE

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Objective In China, the occurrence rule, mechanisms and prevention measures of diseases under extreme weather are few reported and which (del) only focused (focus) on pathophysiological manifestation rather than molecular mechanism level. So (del) (Thus,) further study in this work will be carried out from molecular cytological level. This study explored (del) the effect of hyperthermia on ventricular cardiomyocytes and the participative roles of classic MAPK - ERK5 pathways on hyperthermia induced cardiomyocytes damage.

Methods Neonatal rat ventricular cardiac myocytes (NRVM) were isolated from the hearts of 1- to 3-day-old Sprague Dawley rats. NRVM were exposed to a hyperthermia (42°C, 60 min) environment. The degree of cell damage was observed at 0, 4, 8, 12, 16, and 24 h after recovery. The effects of hyperthermia on myocardial cells

were probed by evaluating lactate dehydrogenase (LDH) release, cells beating rate and rhythm and viability (assessed by MTS assay). Apoptosis was detected using an annexin V-FITC/propidium iodide (PI) staining binding assay. Using western blot semi-quantitating Bim and extracellular signal-related kinase (ERK5) /phosphorylated extracellular signal-related kinase (p-ERK)(??). Using PD98059 as an inhibitor of MAPK pathways, semi-quantitating Bim by western blot(??).

Results 1. The beating rate of myocardial cells was slightly decreased immediately after temperature recovery, (del)(and) gradually decreased with time prolonged, and the (del)(.) Cell viability was (del) decreased (p<0.05);(and) the activity of lactate dehydrogenase was (del) increased (p<0.05). 2. Based on western blot analysis, the elevation of Bim protein expression occurred at recovery time (8 h) and (del)(,) peaked at 12 h(,) then went down slowly at 24 h after hyperthermia (p<0.05); ERK5 pathway responding to hyperthermia treatment (p<0.05). 3. Levels of Bim slightly decreased at (in) PD98059 group compared with hyperthermia group (p<0.05).

Conclusions Hyperthermia induces myocardial cells damage with apoptosis as main type. ERK5 participated the injure process of hyperthermia and Bim played its role via a MAPK-ERK5 pathway.

e0186 STUDY ON THE MECHANISM OF INHIBITORY EFFECT OF CTLA-4IG FUSION PROTEIN ON ATHEROSCLEROSIS IN APOE DEFICIENT MICE

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Objective To investigate the mechanism of inhibitory effect of CTLA-4Ig fusion protein on atherosclerosis in mice with an apolipoprotein-E gene defect fed on cholesterol diet.

Methods 30 male 10-week-old apoE(-/-) mice were fed on cholesterol diet and divided into CTLA-4Ig treatment group, IgG1 group and PBS group at random, 10 in each. The three groups were given intraperitoneal injection of CTLA-4Ig (10 µg per time), Rat-IgG1 (10 µg per time), (and) PBS (100 µl per time) respectively, twice a week, for 12 weeks. Followed by a 12-week treatment, the whole aorta from the root to crotch of iliac artery was separated after anaesthesia with the intraperitoneal injection of 1% pentobarbital and the whole (total) blood was taken to obtain serum. Subsequently, the area ratio of plaque and lumen, the thickness ratio of endangium and tunica media, the lipid-soaking extent intra-plaque and the content of collagen fibrils and smooth muscle cells intra-plaque were analysed by image-processing soft. The serum concentration of total cholesterol, CRP, sICAM-1, IFN-γ, IL-10, and TGF-β1 were measured.

Results There were typical atherosclerotic plaque in apoE(-/-) mice fed on cholesterol diet after 12 weeks and it was light in the CTLA-4Ig group. There were statistical value of difference in the area ratio of plaque and lumen, the thickness ratio of endangium and tunica media, the lipid-soaking extent intra-plaque, and the content of collagen fibrils in three groups (p all<0.05). It was found that the area ratio of plaque and lumen, the thickness ratio of endangium and tunica media, and the lipid-soaking extent intra-plaque were significant lower and the content of collagen fibrils was higher in the CTLA-4Ig group than those in the IgG1 group and PBS group (p all<0.05), but there was no significant difference in those between the IgG1 group and PBS group (p all>0.05). There were no significant difference in content of smooth muscle cells in three groups (p>0.05). There were no significant difference in serum concentration of total cholesterol in three groups (p>0.05). There were statistical value of difference in the serum concentration of CRP,

sICAM-1, IFN- γ , IL-10, and TGF- β 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- γ and increase IL-10 and TGF- β 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 μ 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 α subunit mRNA abundance decreased dramatically in paced group ($p<0.05$). Enalapril and irbesartan prevented the decrease of Nav1.5 α subunit mRNA expression compared with paced group ($p<0.05$). Ang-(1-7) had no effects on the decrease of Nav1.5 α 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